



UNIVERSIDADE DE SÃO PAULO

FACULDADE DE MEDICINA DE RIBEIRÃO PRETO



CURSO DE MEDICINA - 2017

RESISTÊNCIA À INSULINA

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**Departamento de Fisiologia
FMRP-USP**

Definição de Resistência à Insulina



É o fator etiológico chave do diabetes tipo 2 que se caracteriza por alterações em diversos pontos da via de transmissão do sinal da insulina e que está diretamente relacionada à obesidade.

Doenças com fator de risco relacionado à obesidade

- Doenças Cardiovasculares
- Diabetes Mellitus tipo 2
- Distúrbios ósseos
- Esteatose hepática
- Neoplasias, etc.

$$\text{IMC} = \frac{\text{Peso}}{(\text{Altura} \times \text{Altura})}$$

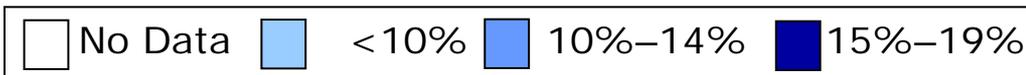
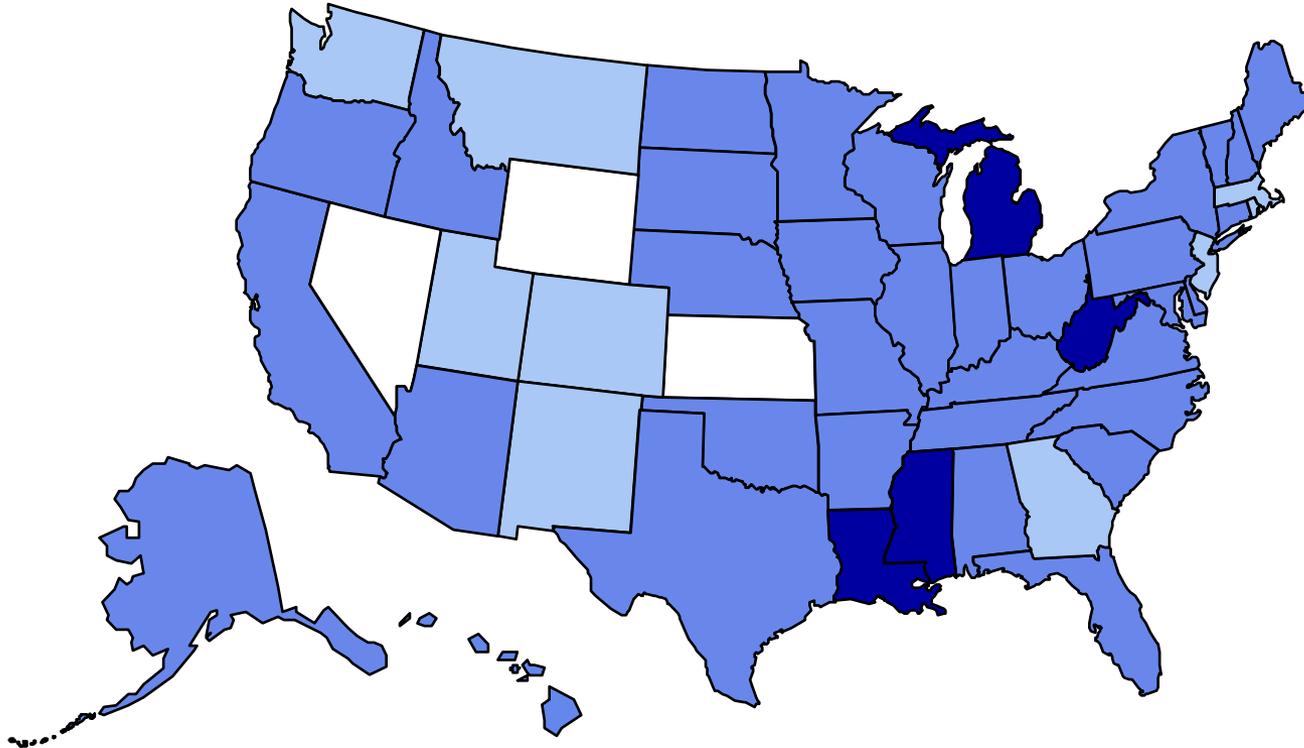
Exemplo de como calcular o Índice de Massa Corporal (IMC):
80kg / 1,80m x 1,80m = 24,69 (Normal)

Categoria	IMC	Peso Saudável equivale ao peso Normal.
Abaixo do peso	Abaixo de 18,5	
Peso normal	18,5 - 24,9	
Sobrepeso	25,0 - 29,9	
Obesidade Grau I	30,0 - 34,9	
Obesidade Grau II	35,0 - 39,9	
Obesidade Grau III	40,0 e acima	

Obesity Trends* Among U.S. Adults

BRFSS, 1991

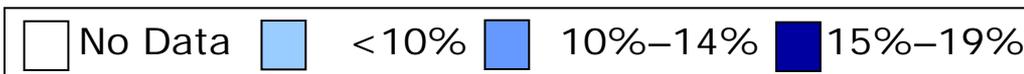
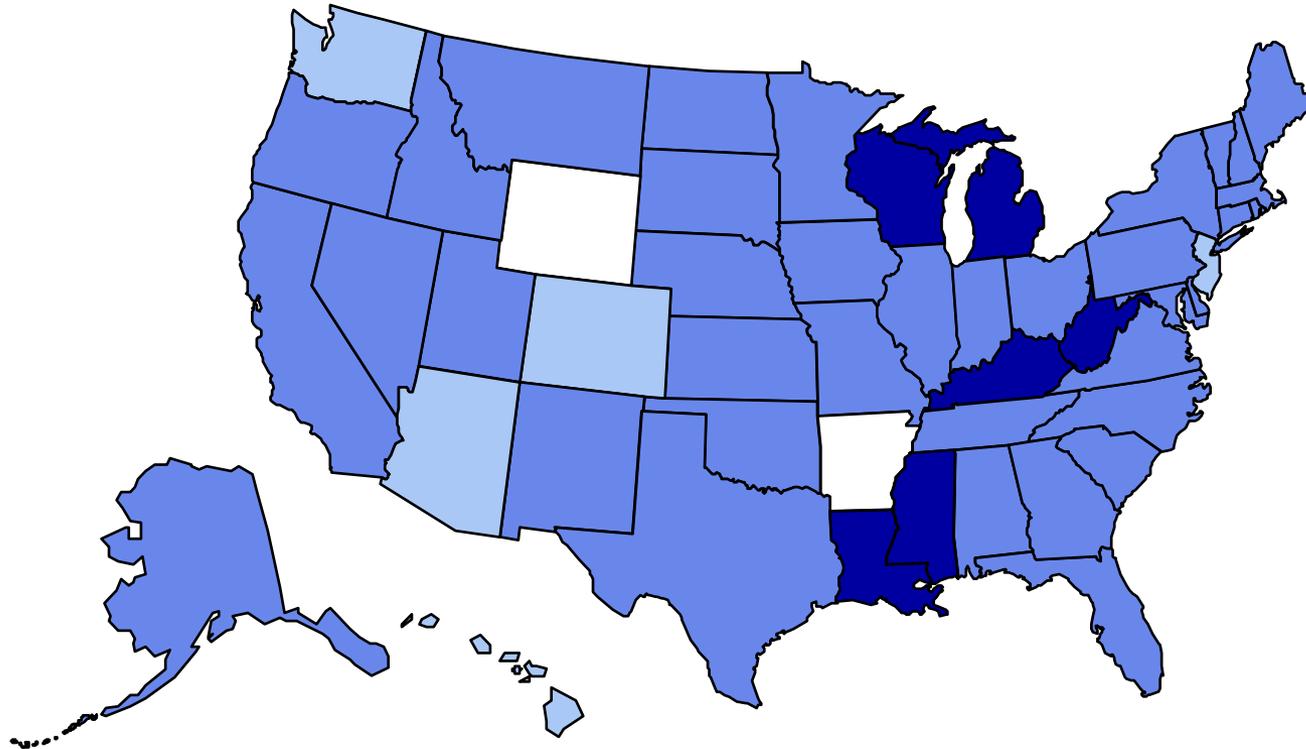
(*BMI ≥ 30 , or ~ 30 lbs overweight for 5' 4" woman)



Obesity Trends* Among U.S. Adults

BRFSS, 1992

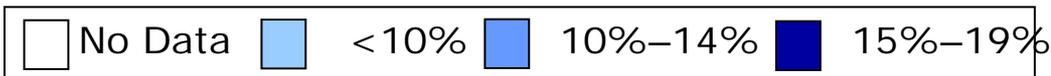
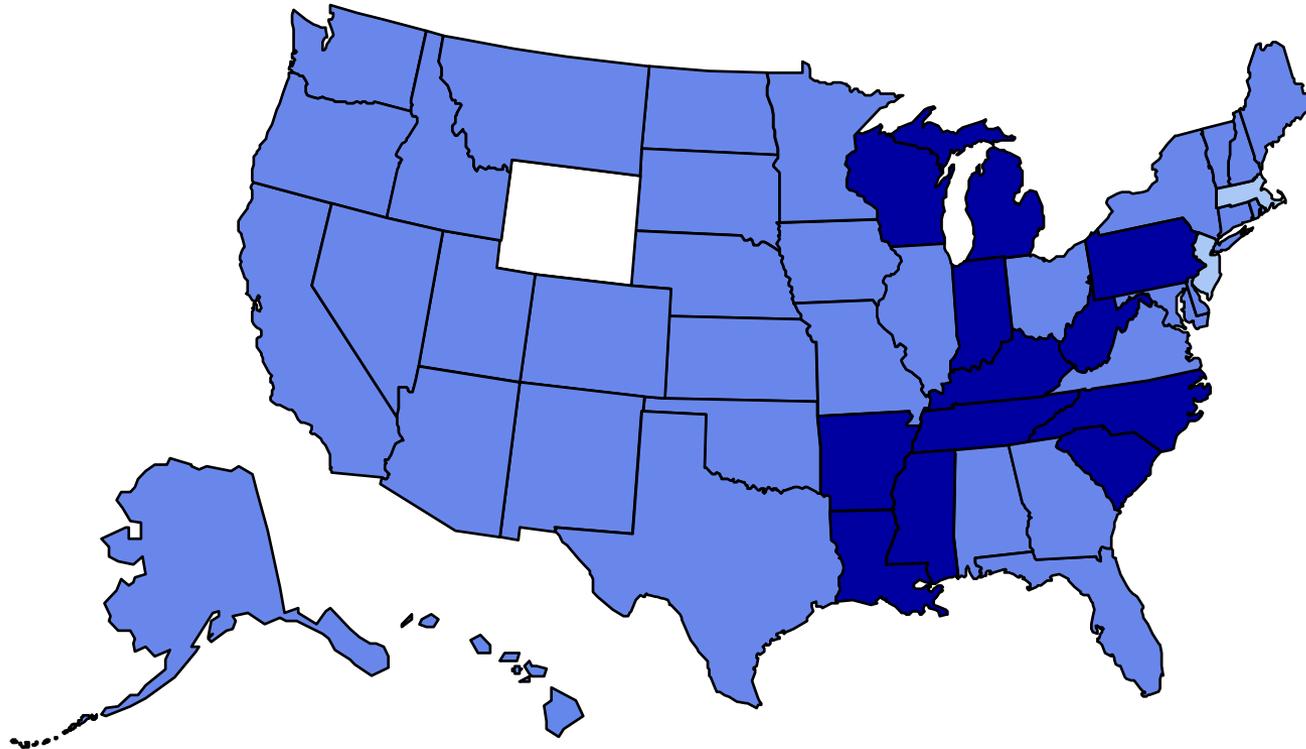
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Obesity Trends* Among U.S. Adults

BRFSS, 1993

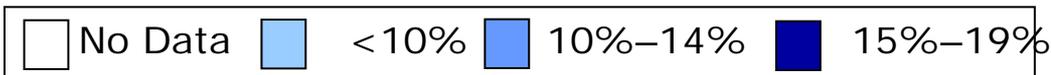
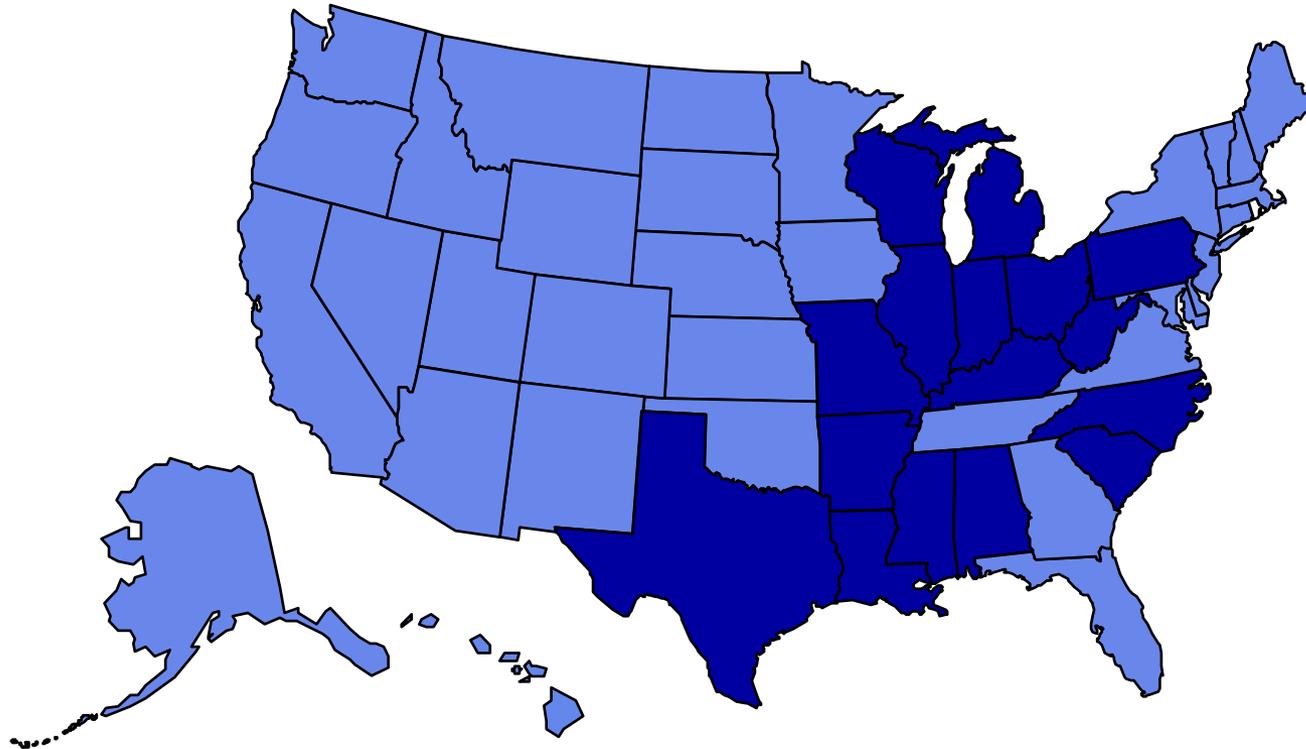
(*BMI ≥ 30 , or ~ 30 lbs overweight for 5' 4" woman)



Obesity Trends* Among U.S. Adults

BRFSS, 1994

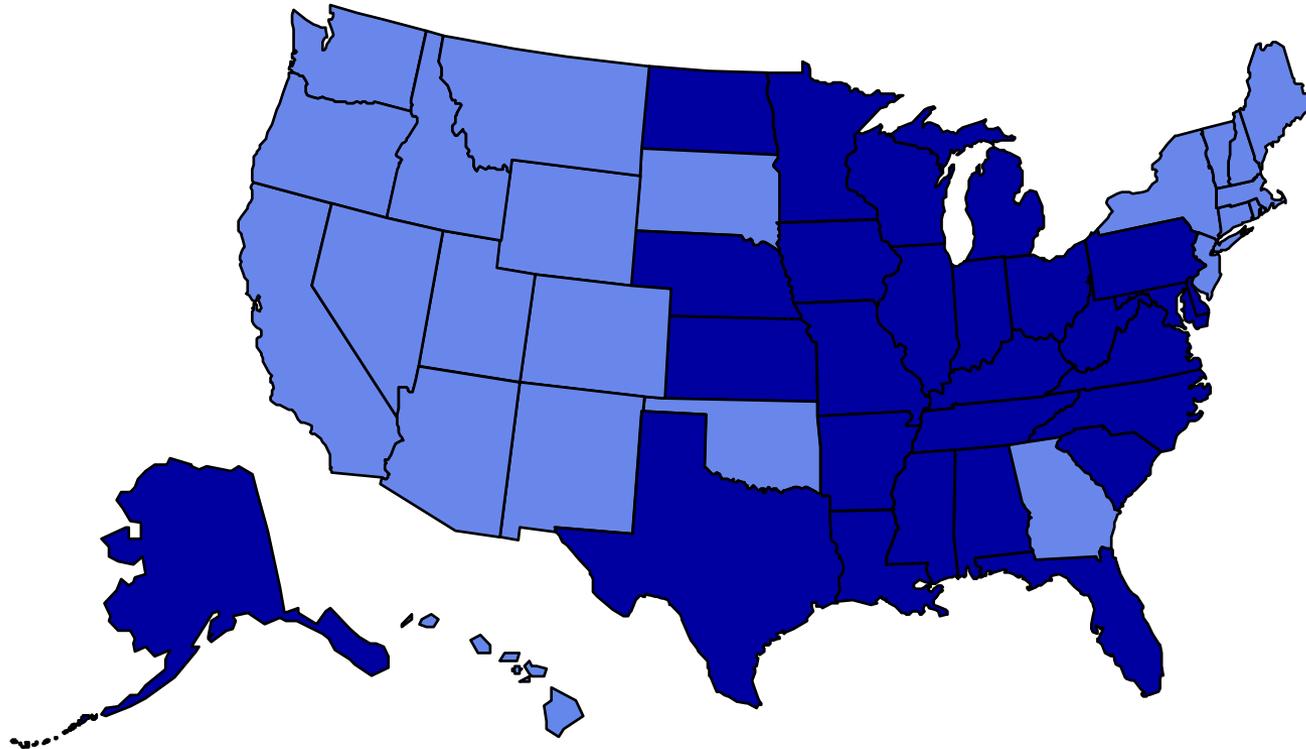
(*BMI ≥ 30 , or ~ 30 lbs overweight for 5' 4" woman)



Obesity Trends* Among U.S. Adults

BRFSS, 1995

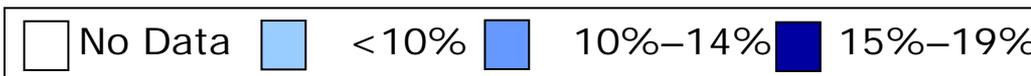
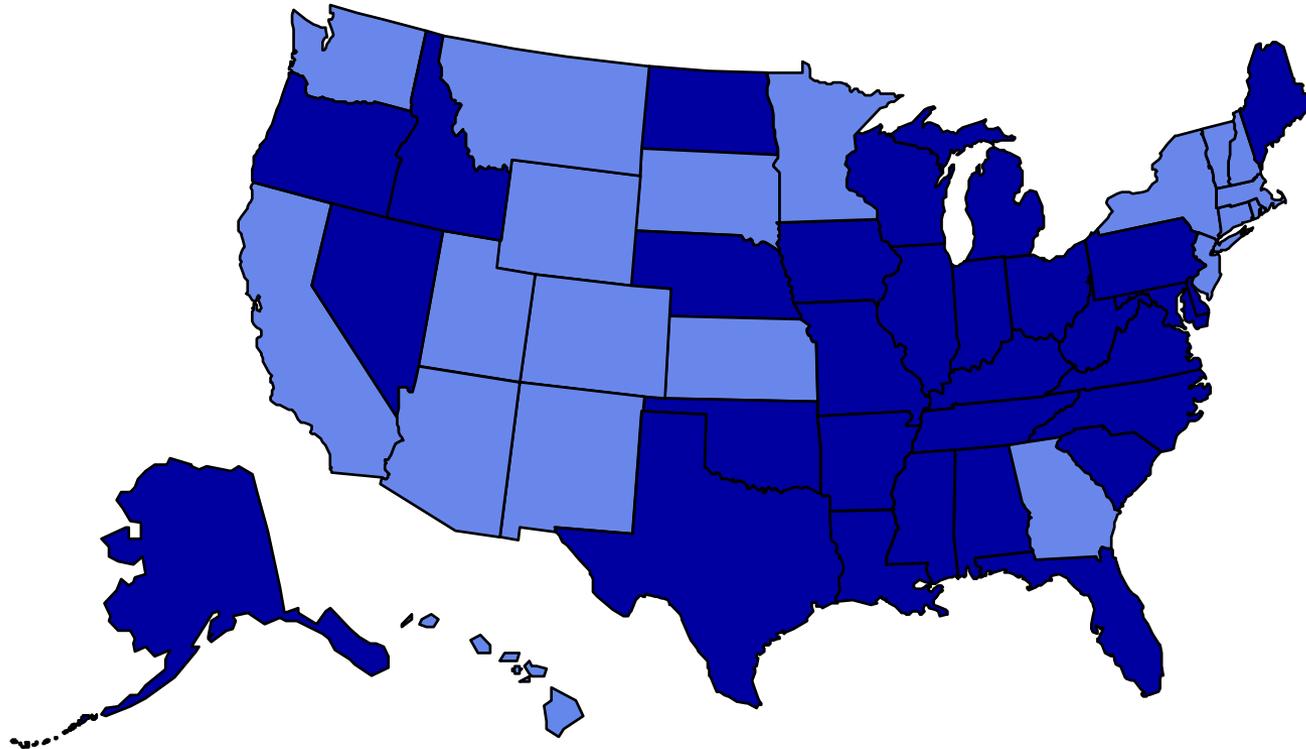
(*BMI ≥ 30 , or ~ 30 lbs overweight for 5' 4" woman)



Obesity Trends* Among U.S. Adults

BRFSS, 1996

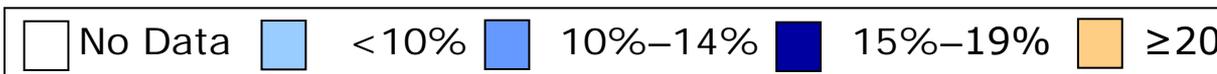
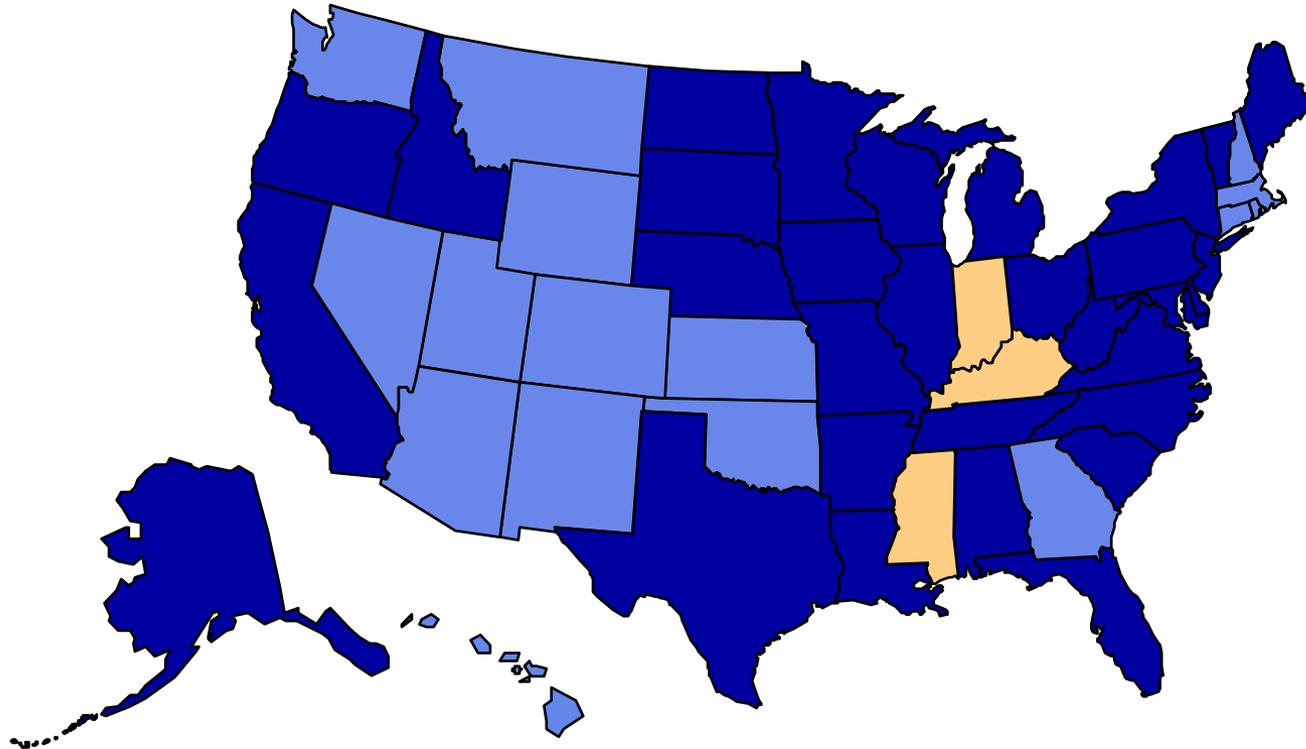
(*BMI ≥ 30 , or ~ 30 lbs overweight for 5' 4" woman)



Obesity Trends* Among U.S. Adults

BRFSS, 1997

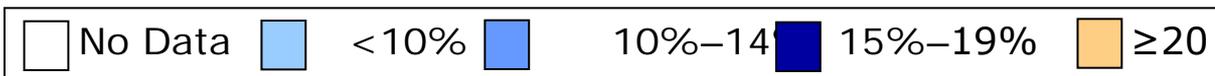
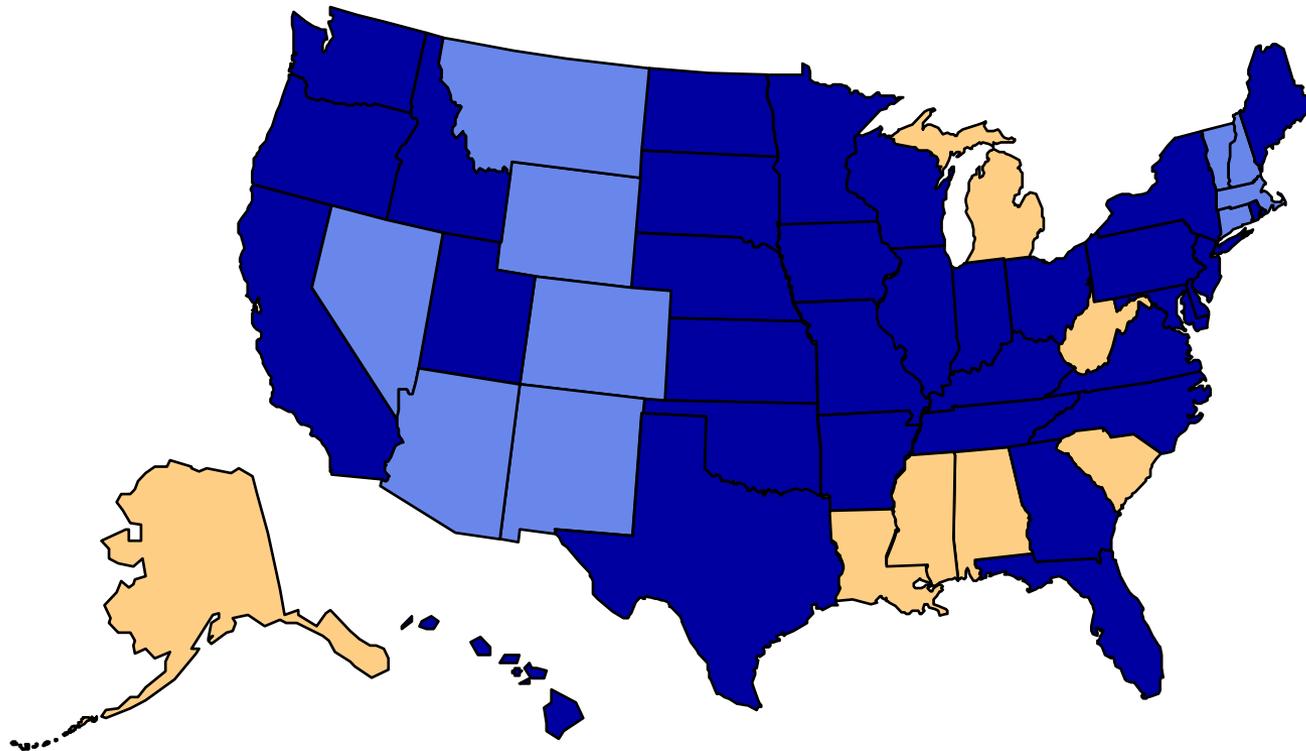
(*BMI ≥ 30 , or ~ 30 lbs overweight for 5' 4" woman)



Obesity Trends* Among U.S. Adults

BRFSS, 1998

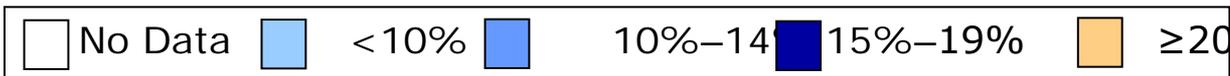
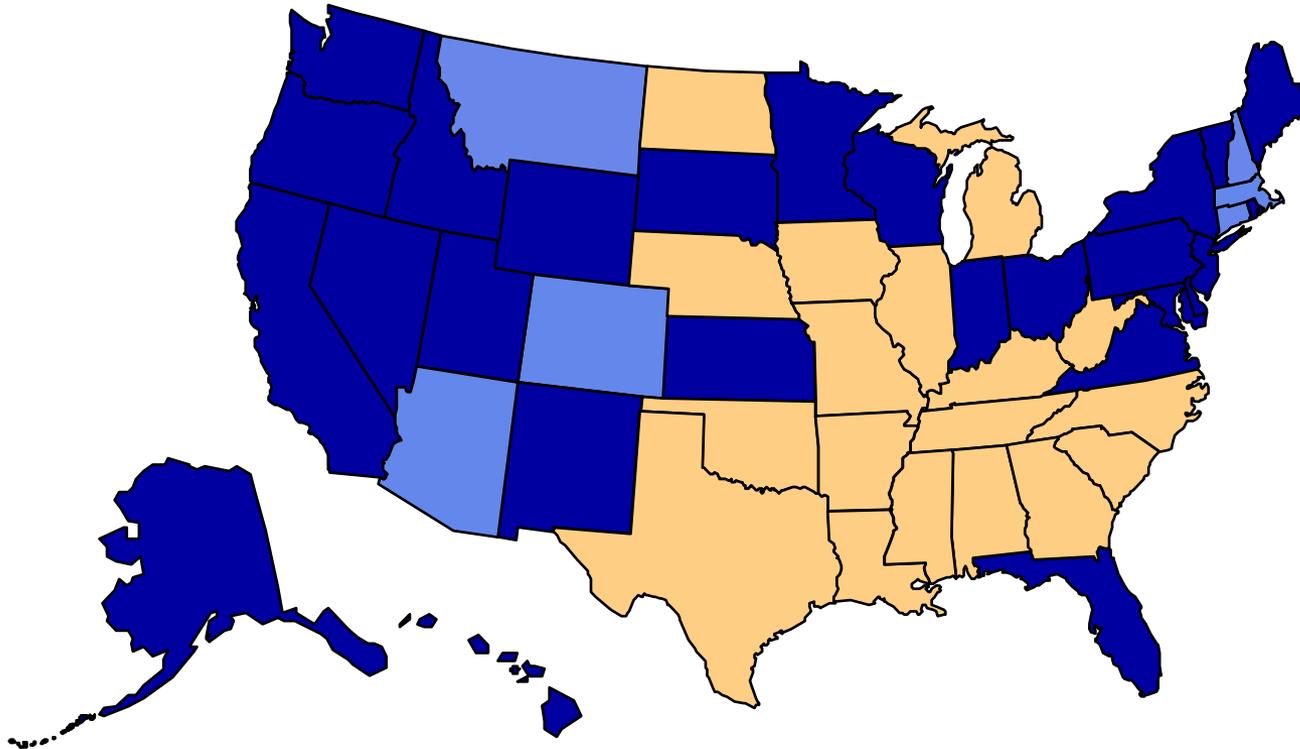
(*BMI ≥ 30 , or ~ 30 lbs overweight for 5' 4" woman)



Obesity Trends* Among U.S. Adults

BRFSS, 1999

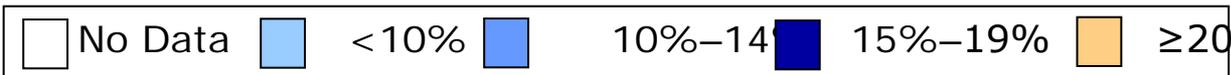
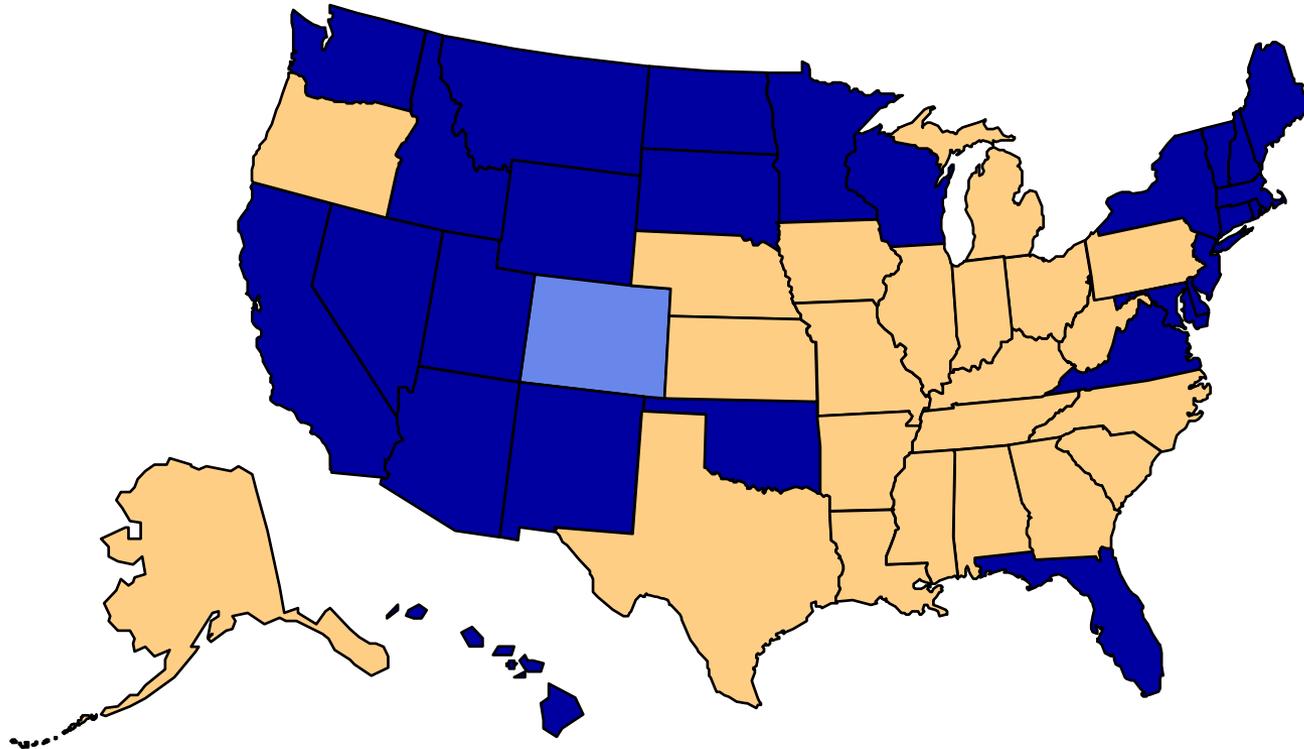
(*BMI ≥ 30 , or ~ 30 lbs overweight for 5' 4" woman)



Obesity Trends* Among U.S. Adults

BRFSS, 2000

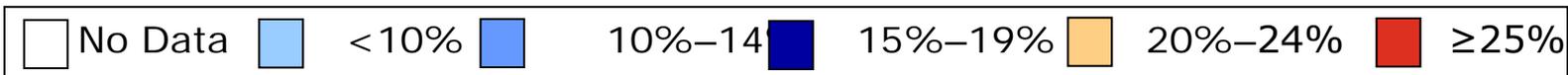
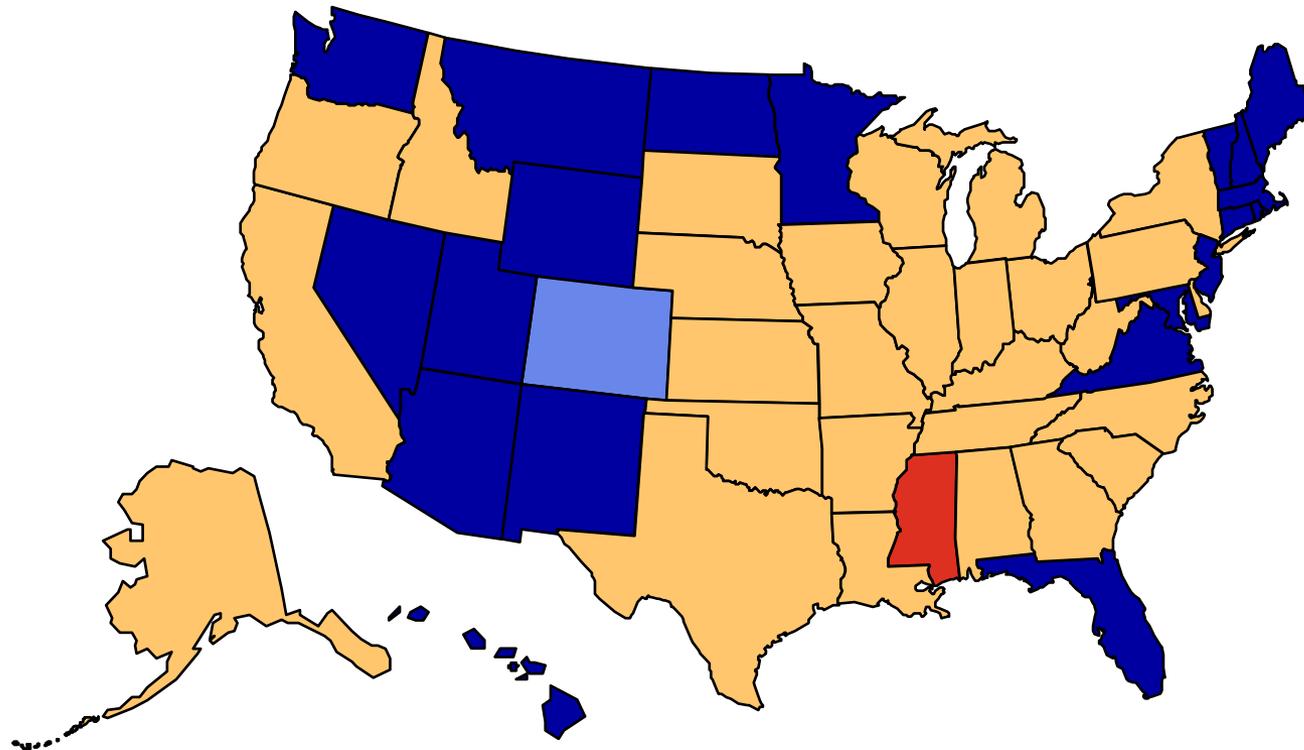
(*BMI ≥ 30 , or ~ 30 lbs overweight for 5' 4" woman)



Obesity Trends* Among U.S. Adults

BRFSS, 2001

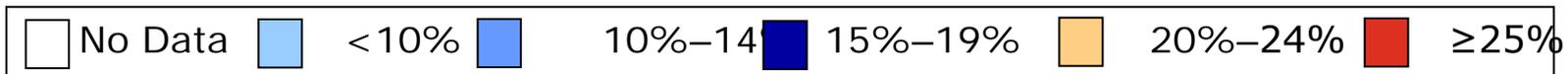
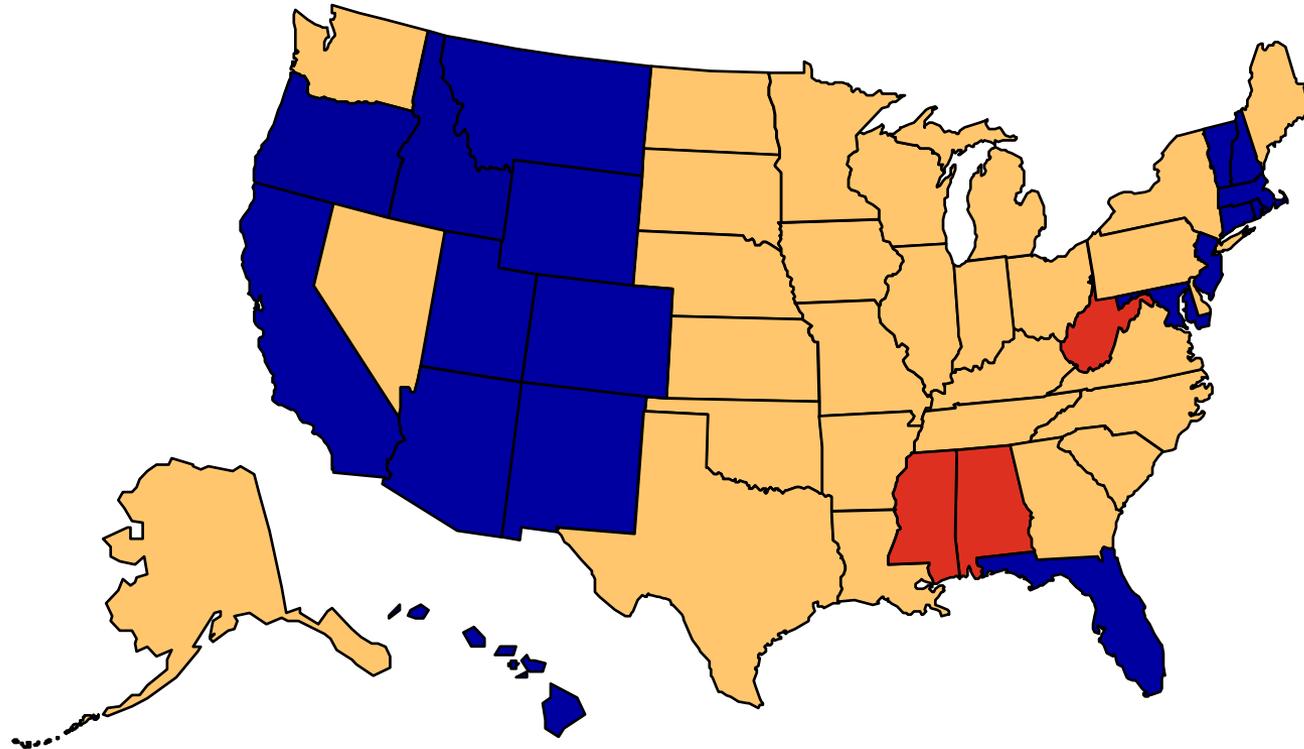
(*BMI ≥ 30 , or ~ 30 lbs overweight for 5' 4" woman)



Obesity Trends* Among U.S. Adults

BRFSS, 2002

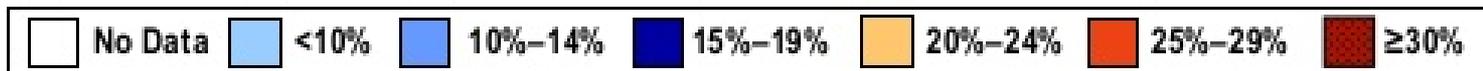
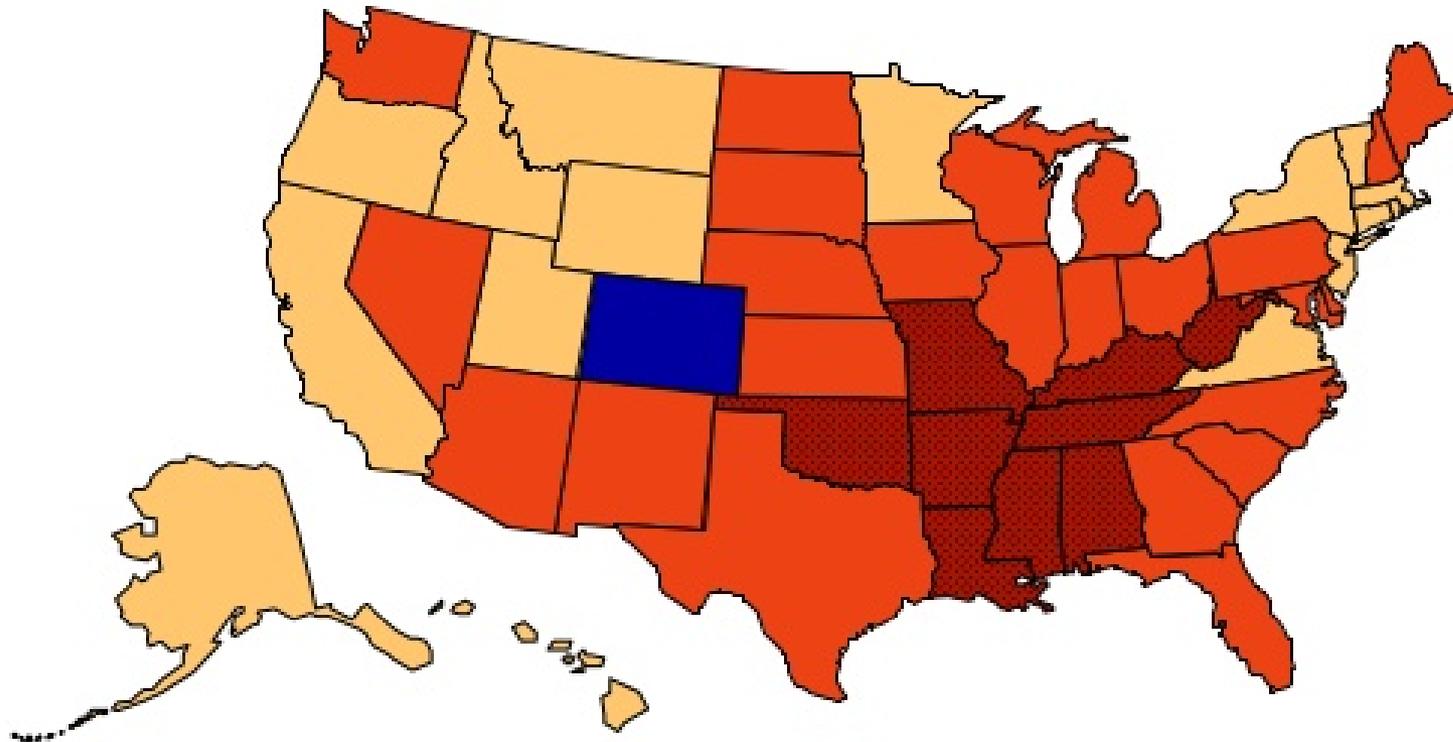
(*BMI ≥ 30 , or ~ 30 lbs overweight for 5' 4" woman)



Source: Behavioral Risk Factor Surveillance System, CDC

Obesity Trends* Among U.S. Adults, BRFSS 2009

(*BMI ≥ 30 , or ~ 30 lbs. overweight for 5' 4" person)



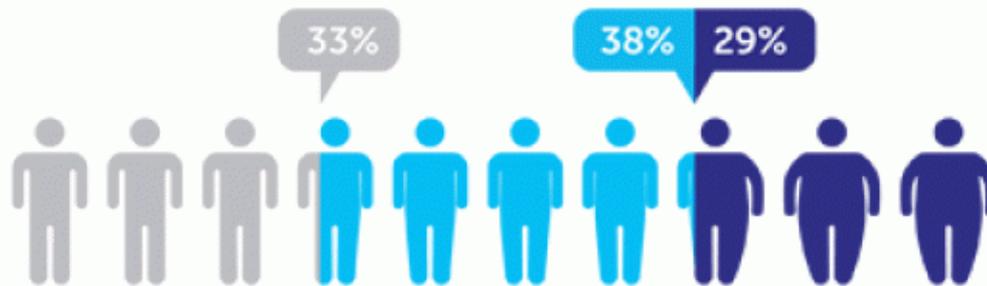
Source: Behavioral Risk Factor Surveillance System, CDC.



IF TRENDS CONTINUE, ALMOST 4 IN 10 ADULTS ARE PREDICTED TO BE OBESE BY 2035

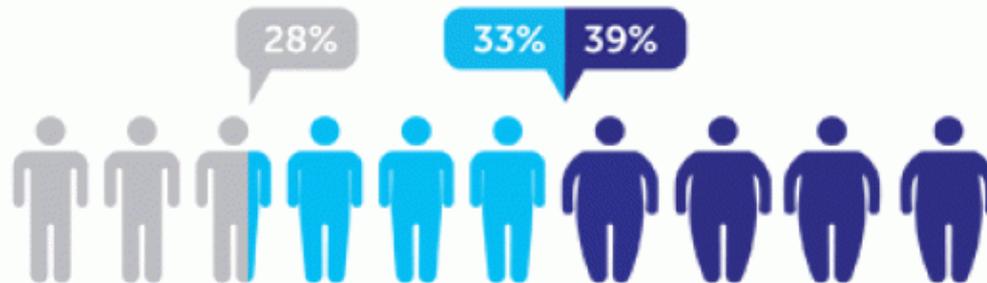
 Healthy Weight  Overweight  Obese

IN
2015

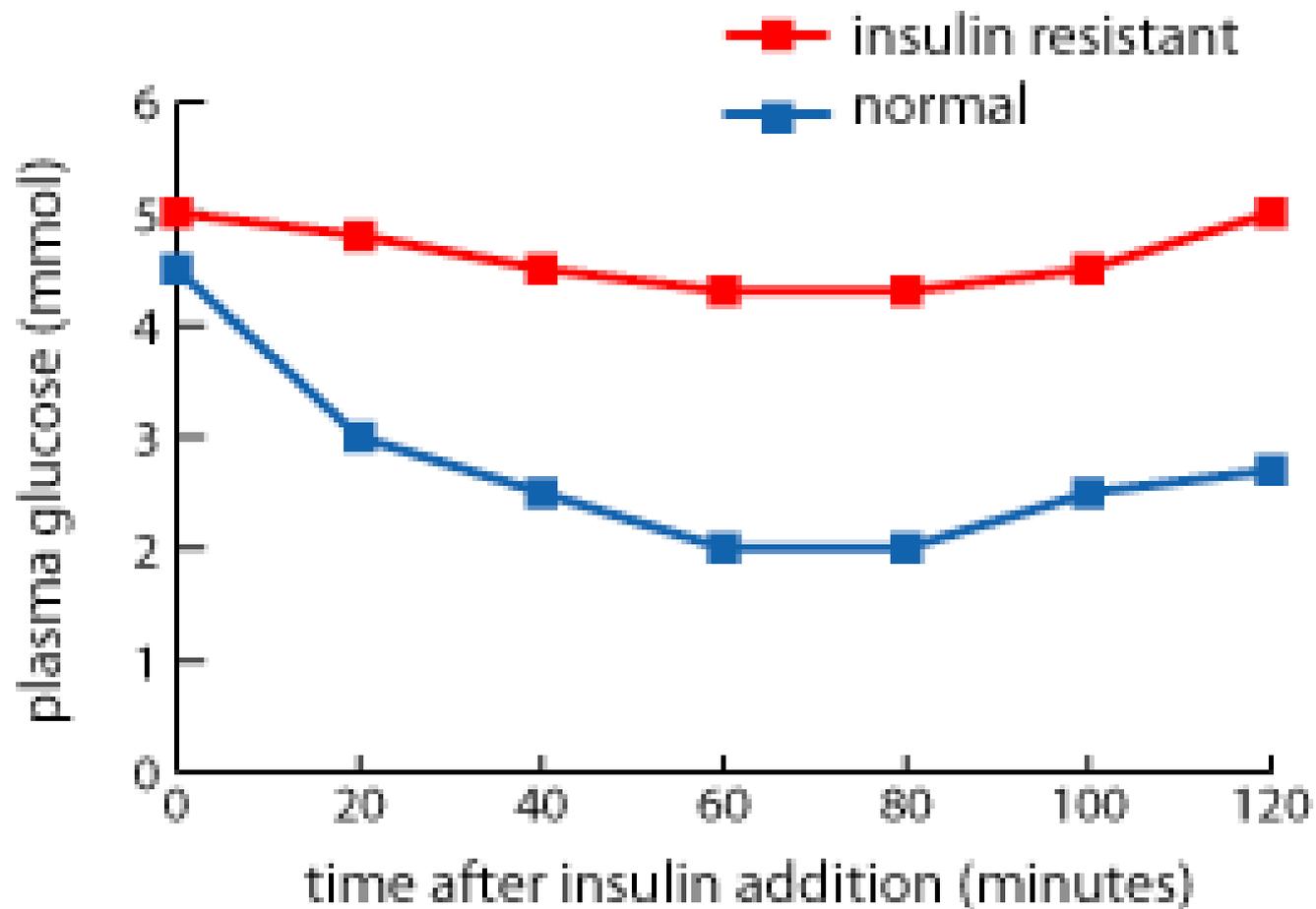


Around **3 in 10** adults are obese.

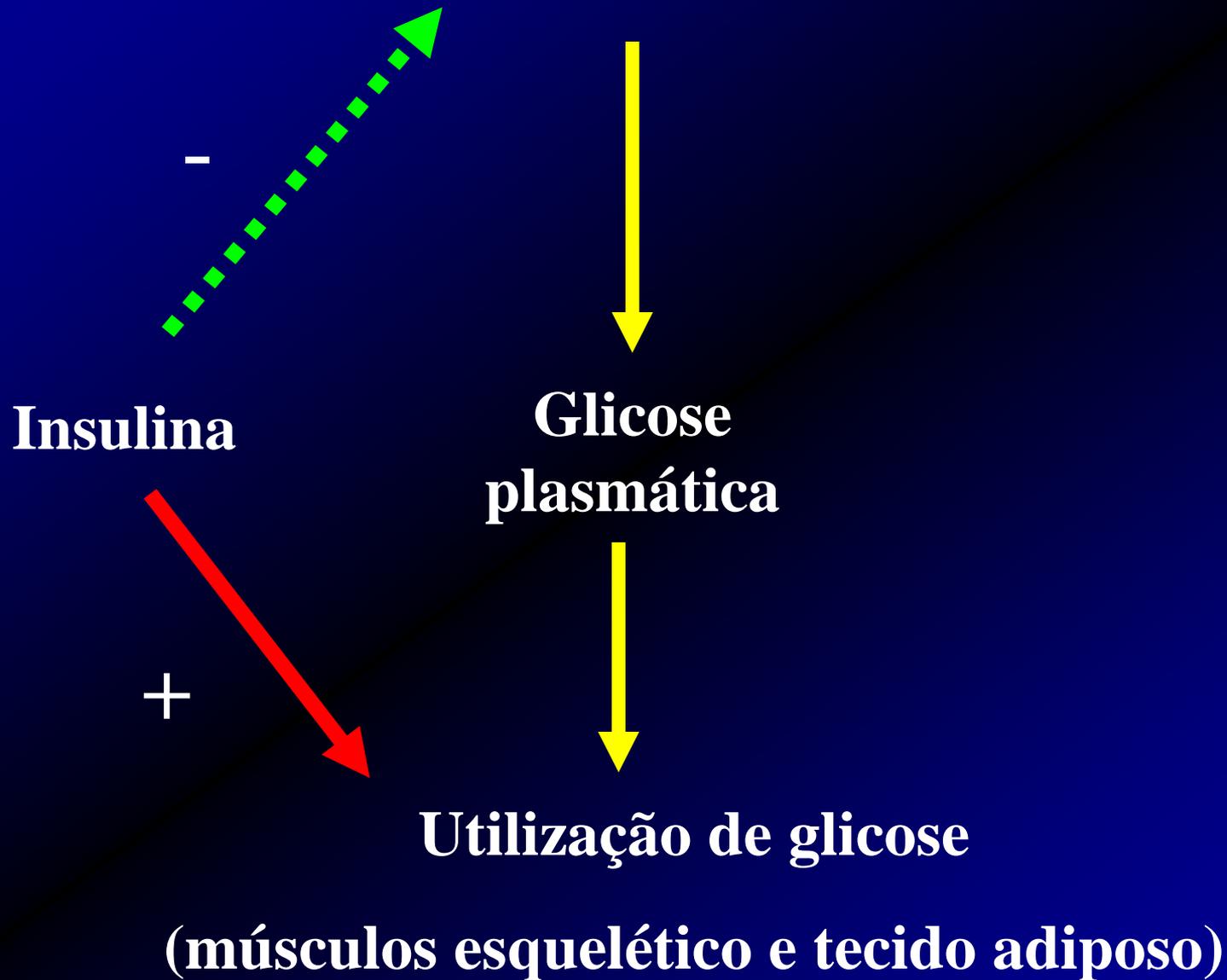
IN
2035



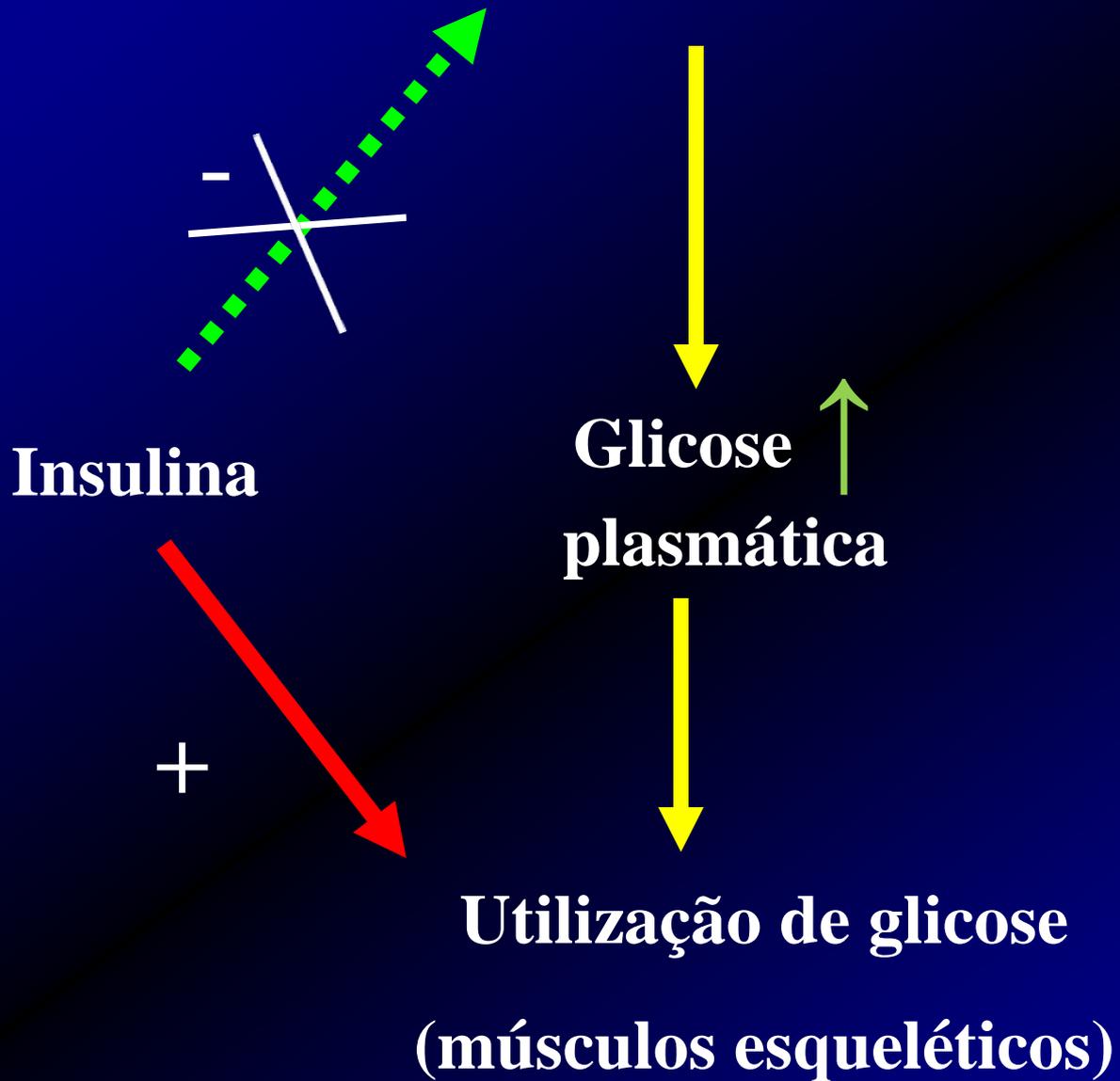
Around **4 in 10** adults will be obese.



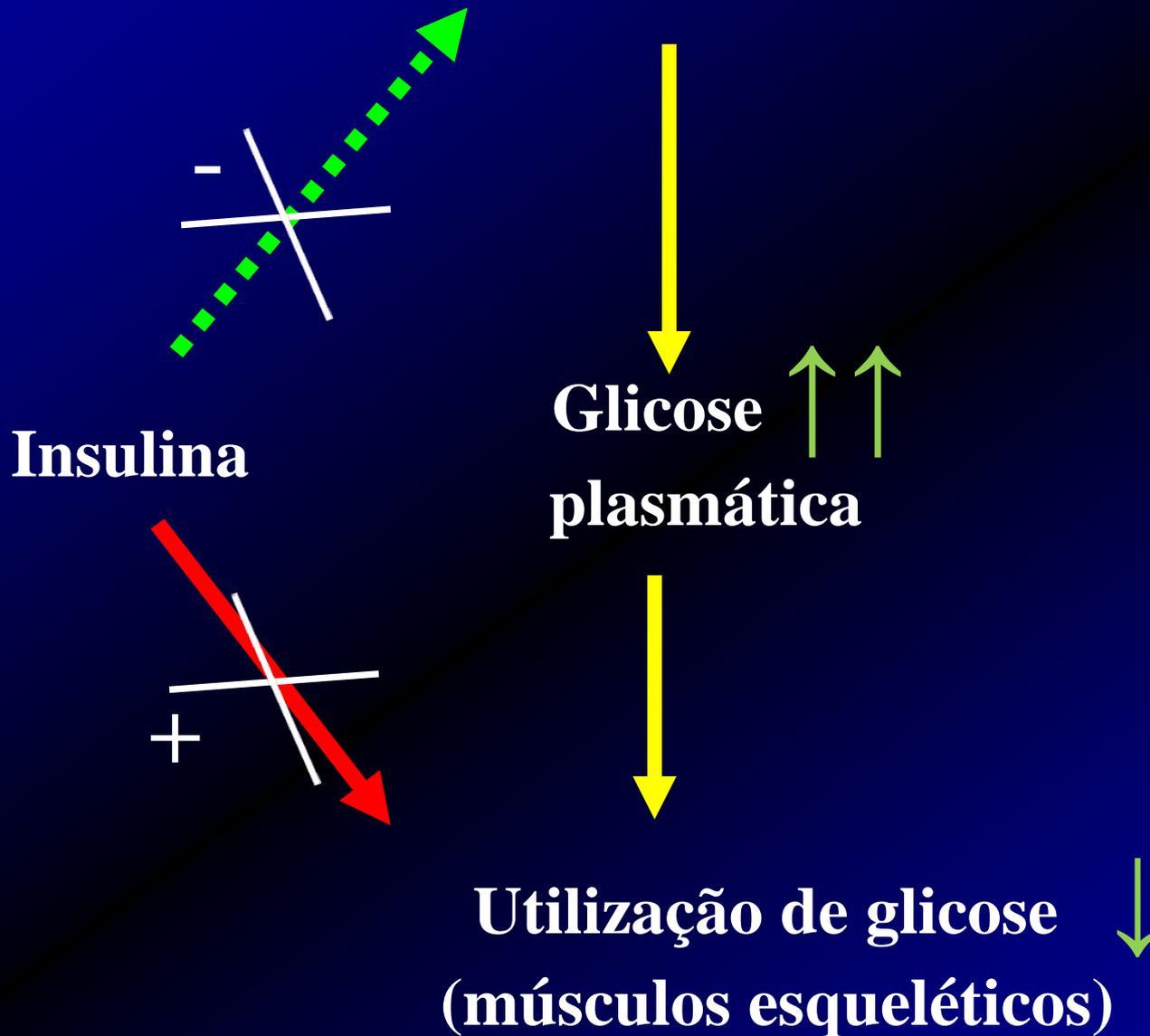
Produção hepática de glicose (Neoglicogênese e Glicogenólise)

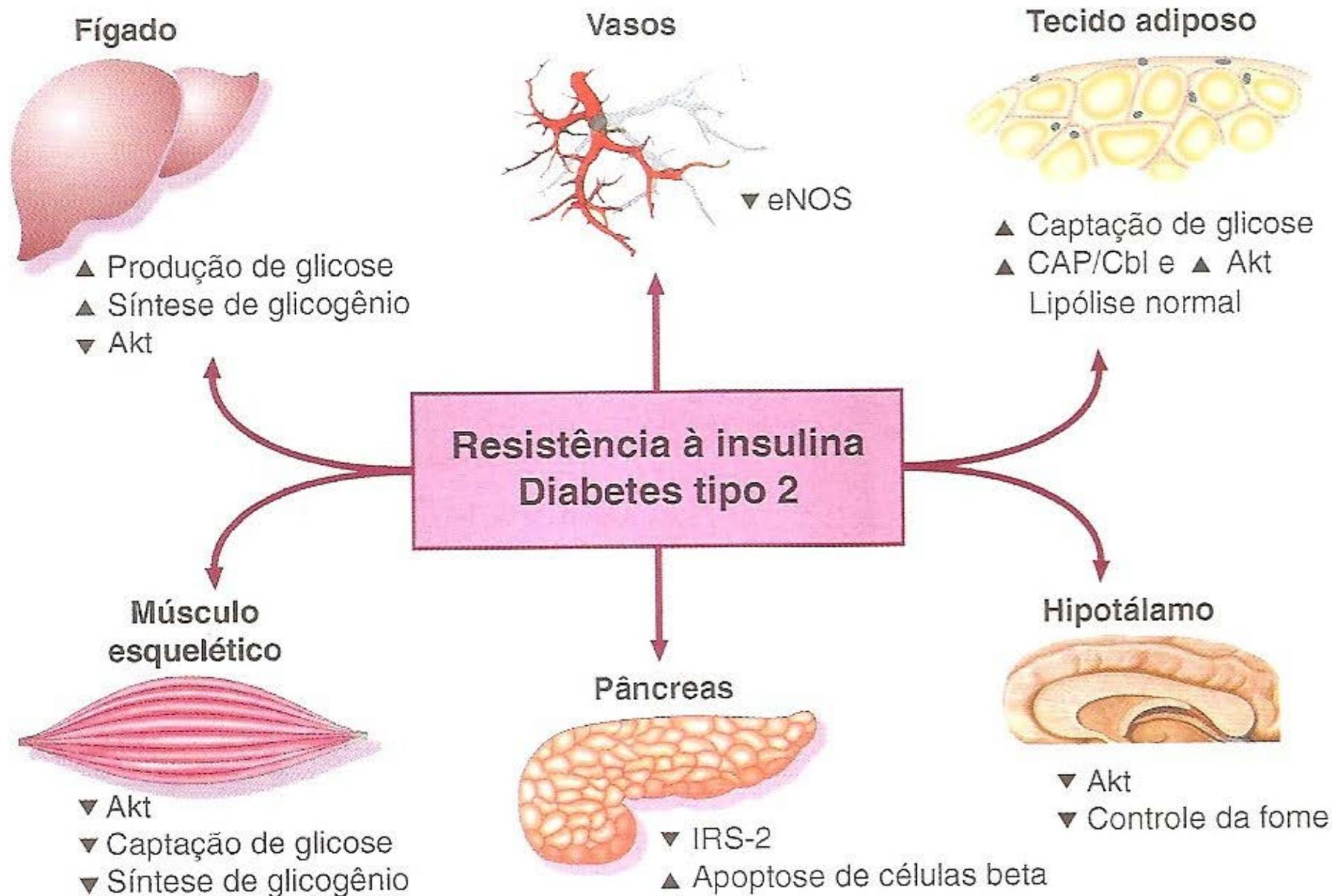


Produção hepática de glicose ↑ (Neoglicogênese e Glicogenólise)



Produção hepática de glicose ↑ (Neoglicogênese e Glicogenólise)



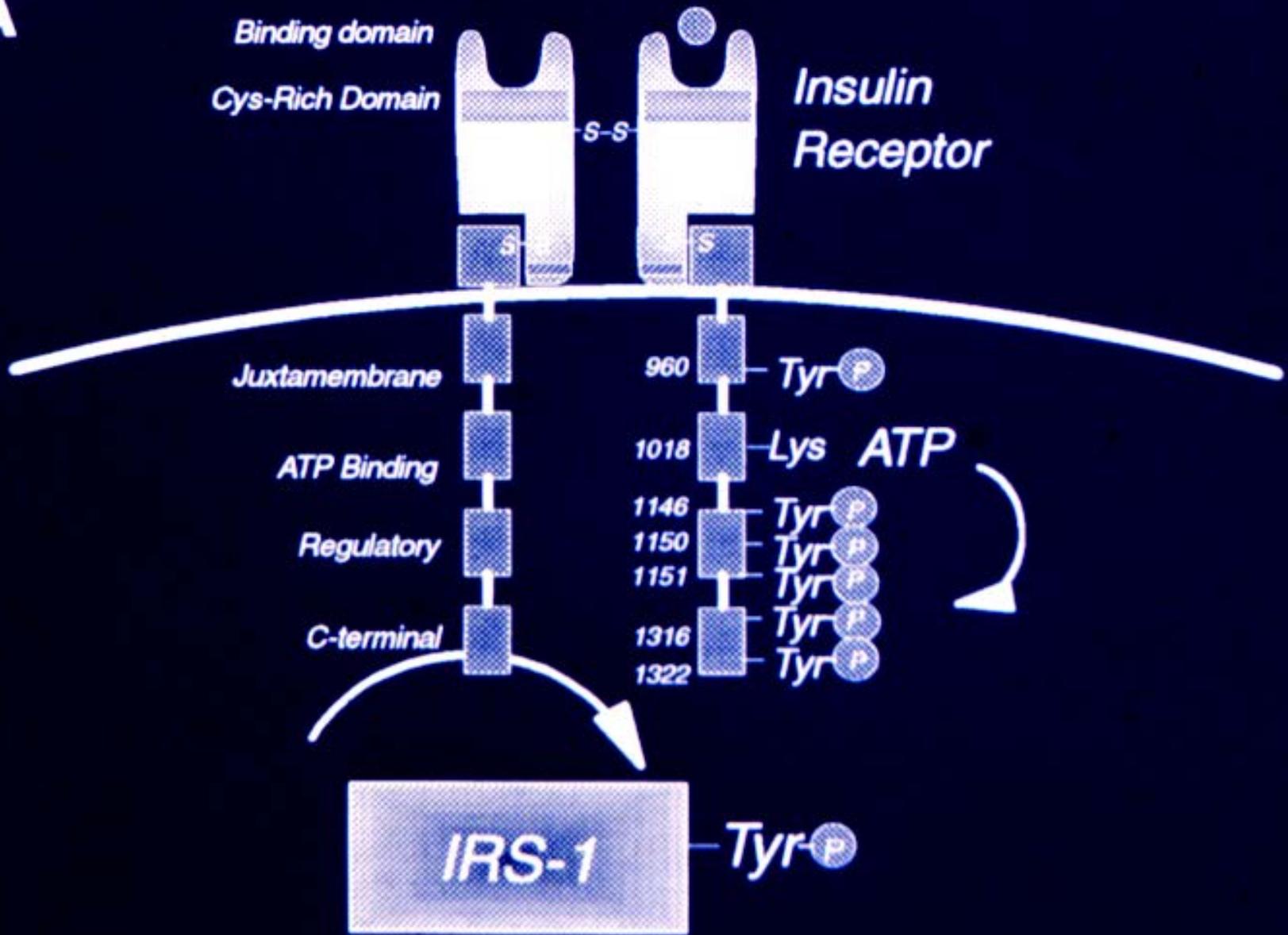


A

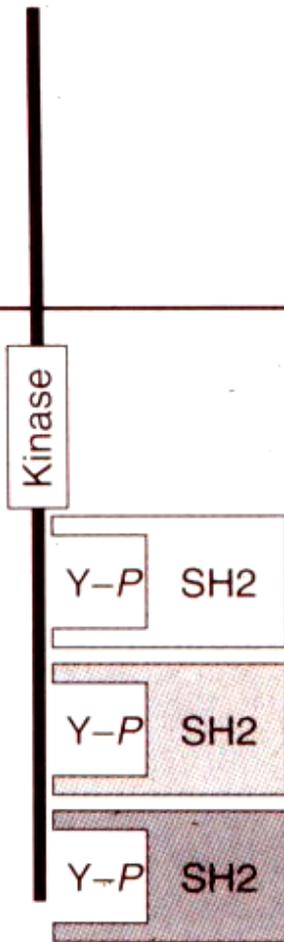
Binding domain
Cys-Rich Domain

Insulin Receptor

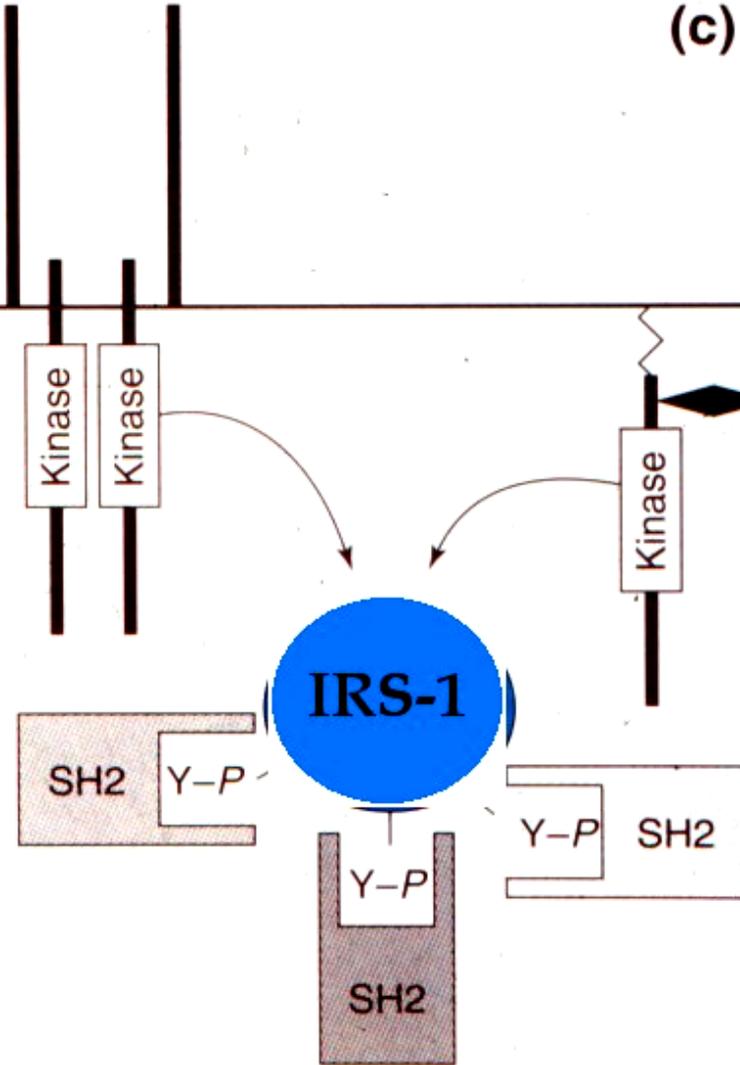
S-S



(a)



(b)

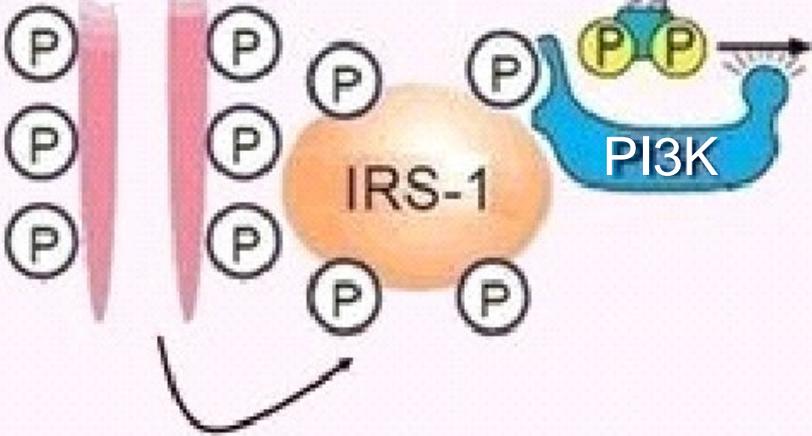


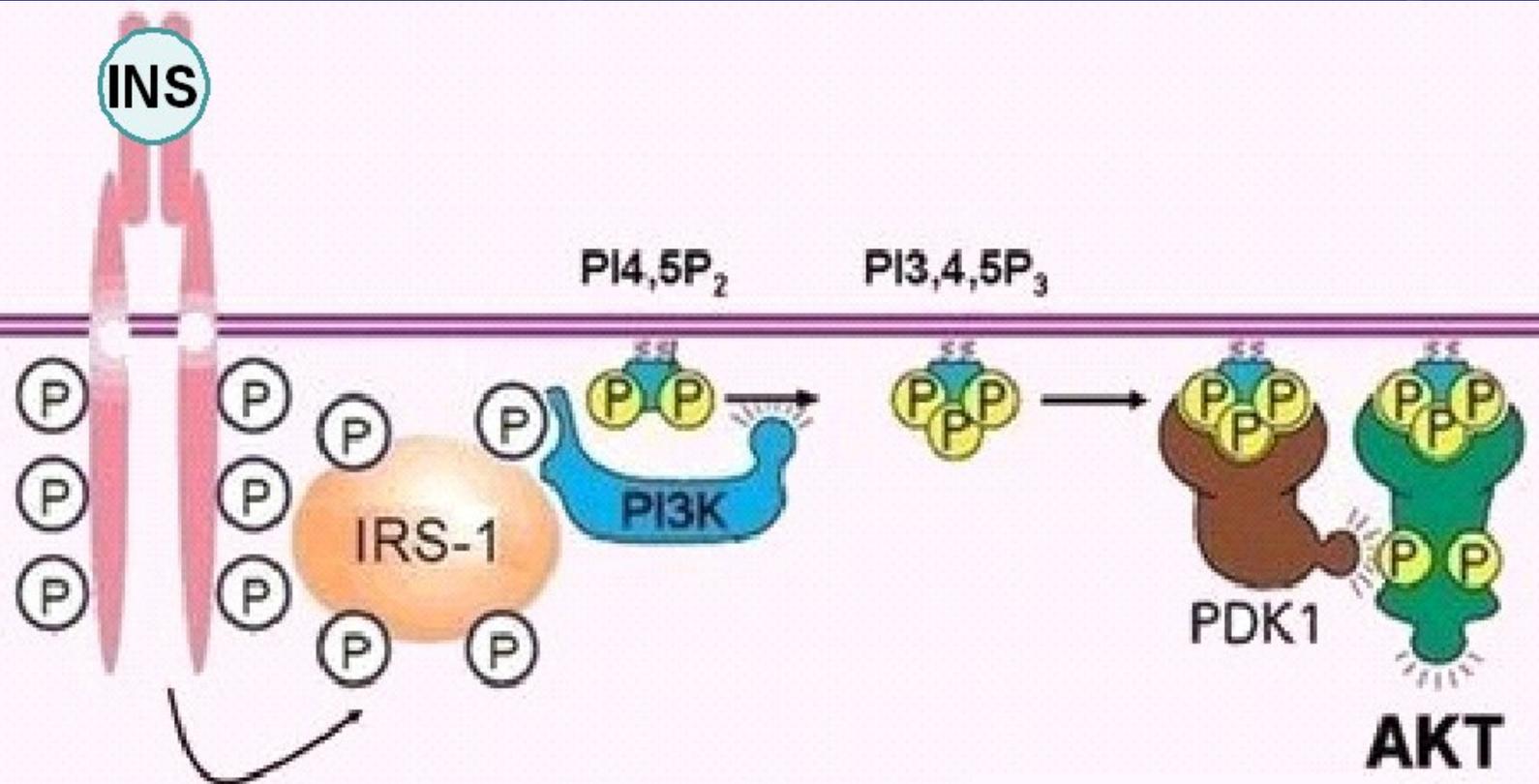
(c)

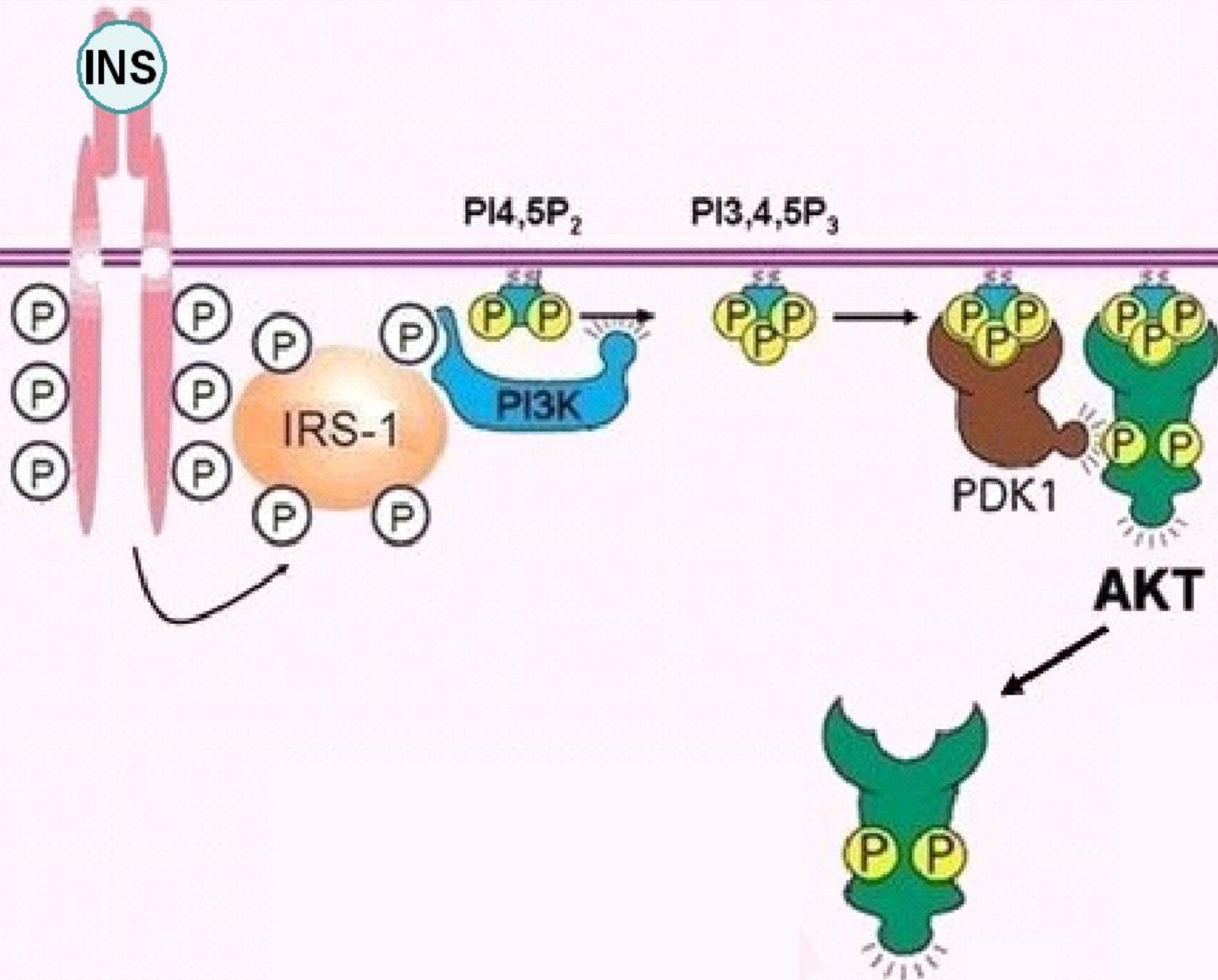


INS

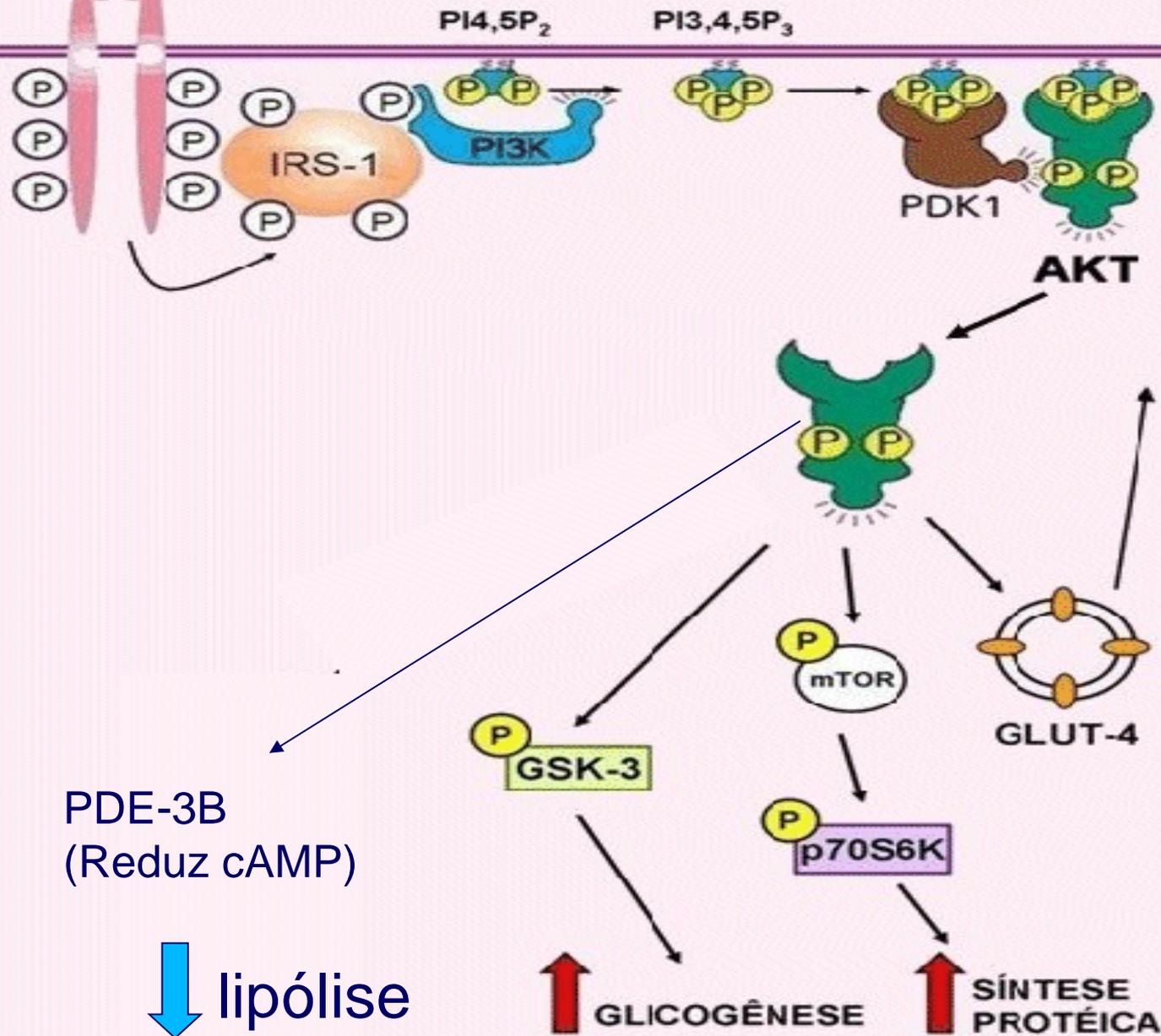
PI4,5P₂



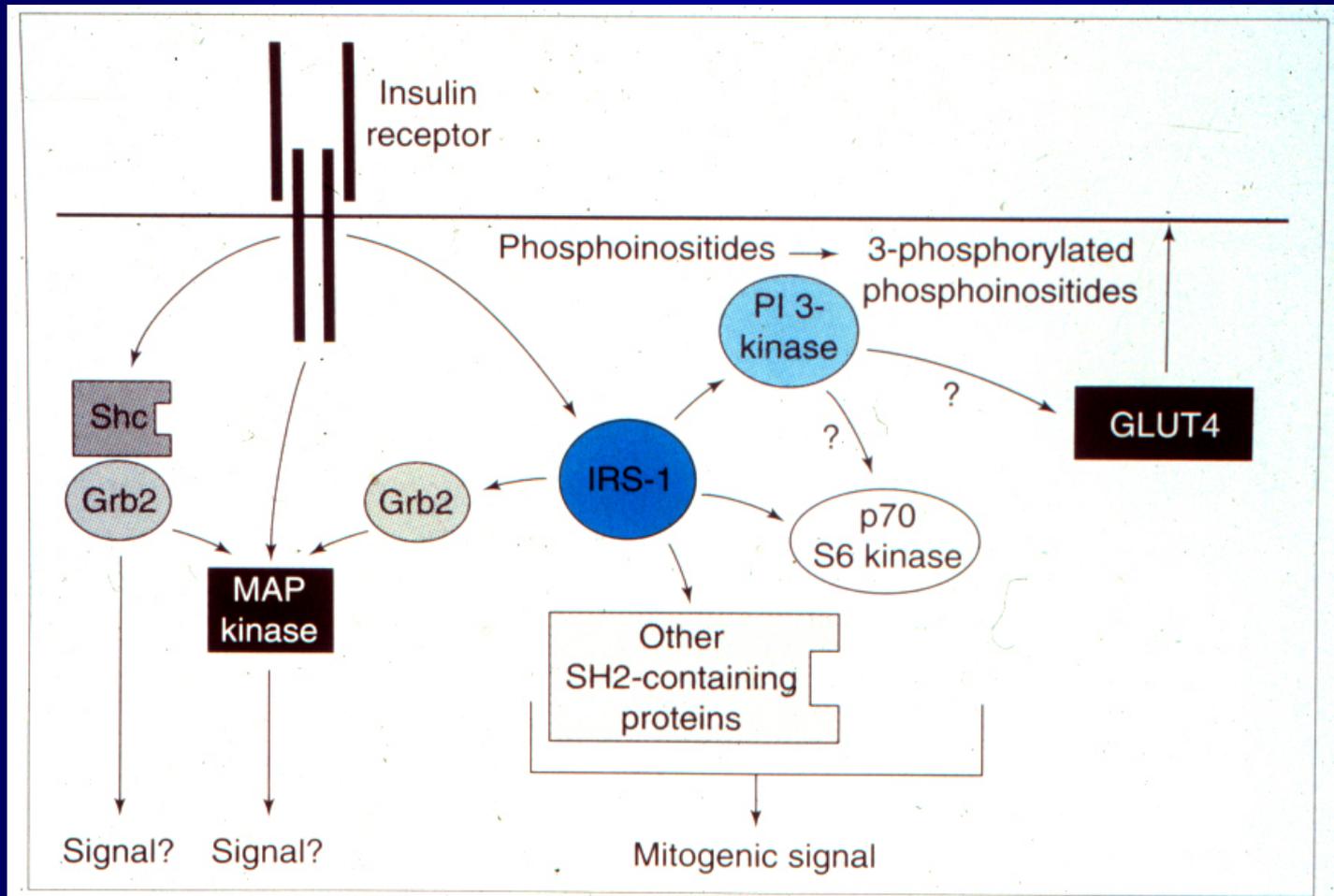




insulina



Ações proliferativas da insulina são mantidas em estados de resistênica

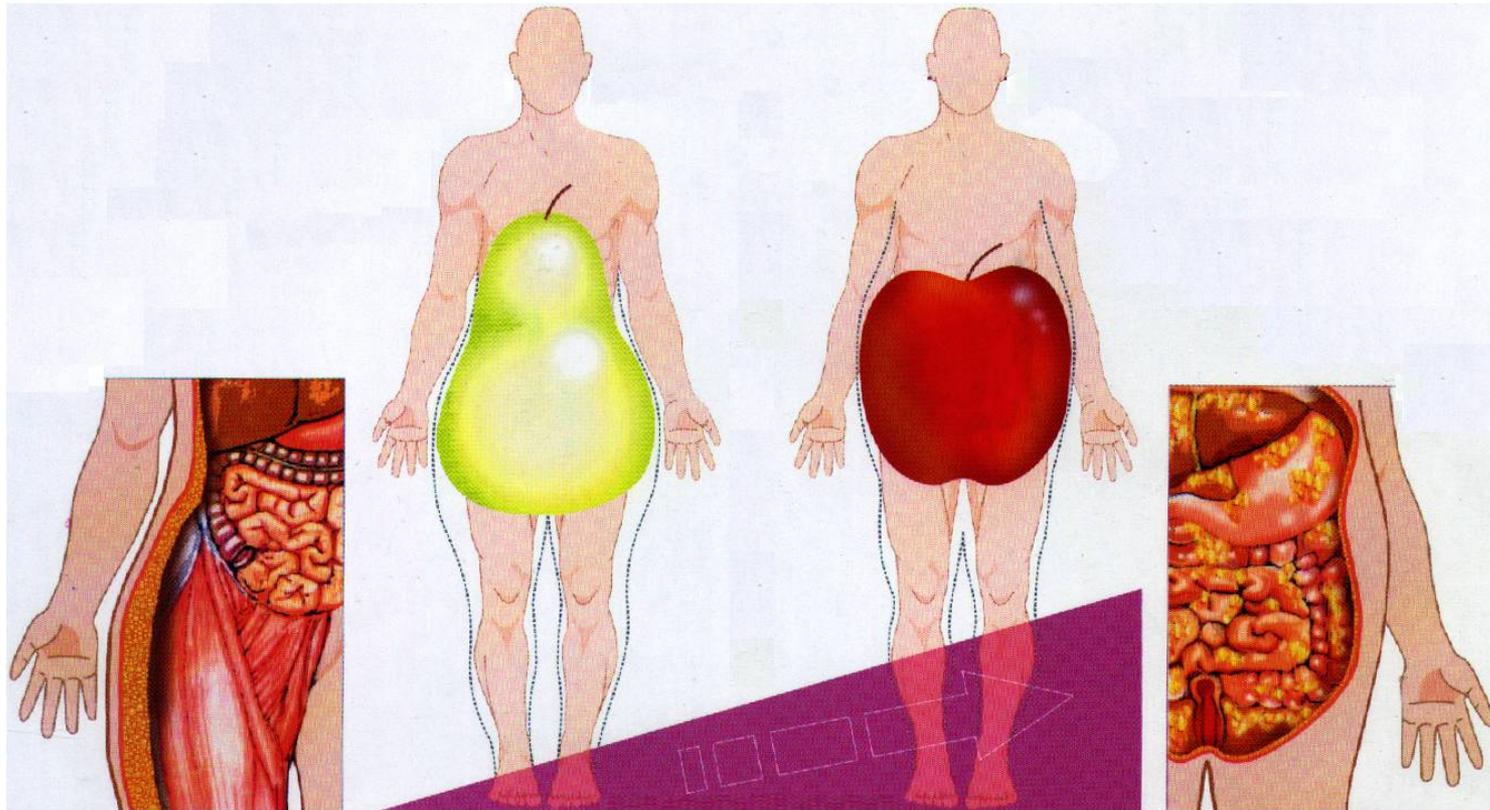


Acanthosis nigricans

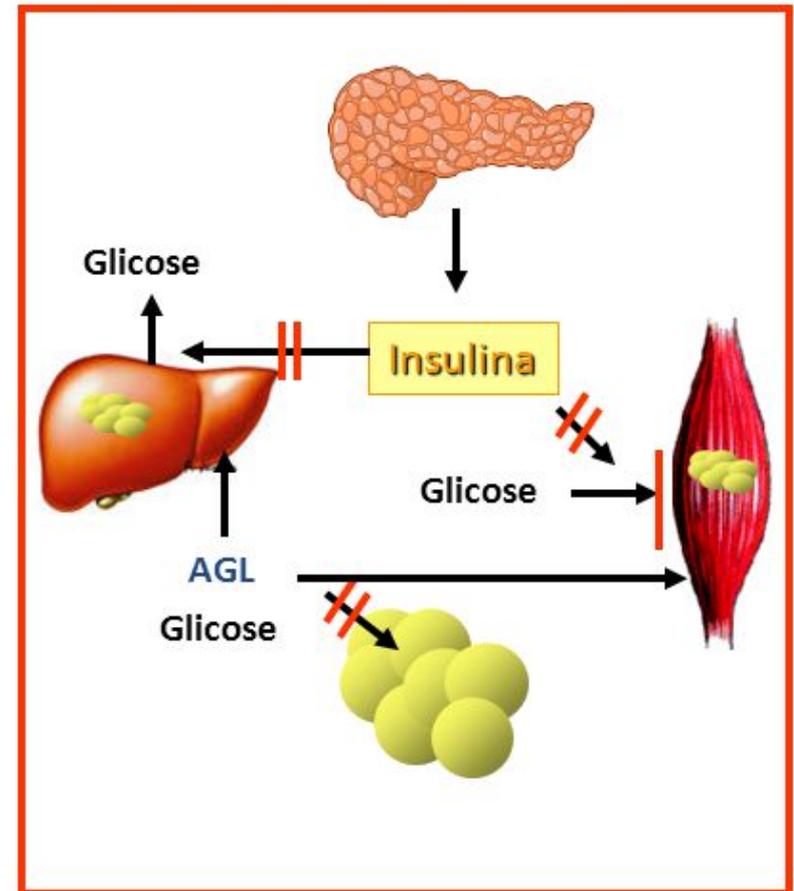
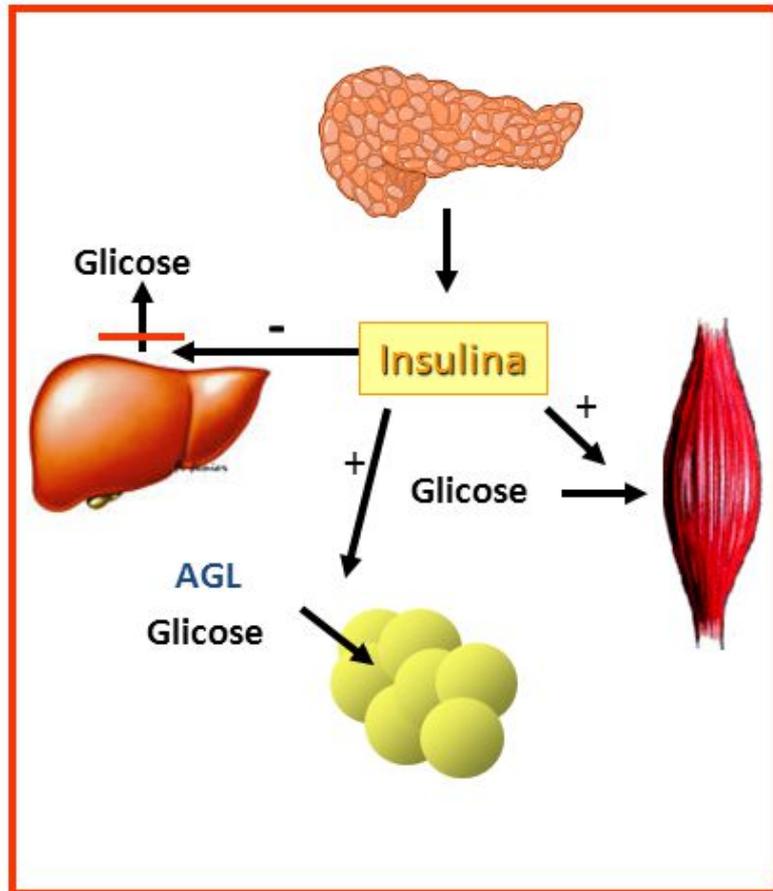


**Por que a obesidade
causa resistência ?**

O Tecido Adiposo Branco Subcutâneo X Visceral



Depósito ectópico de gordura e resistência à insulina



Adaptado de Birbaun M. *Nature* 2001;409:729.

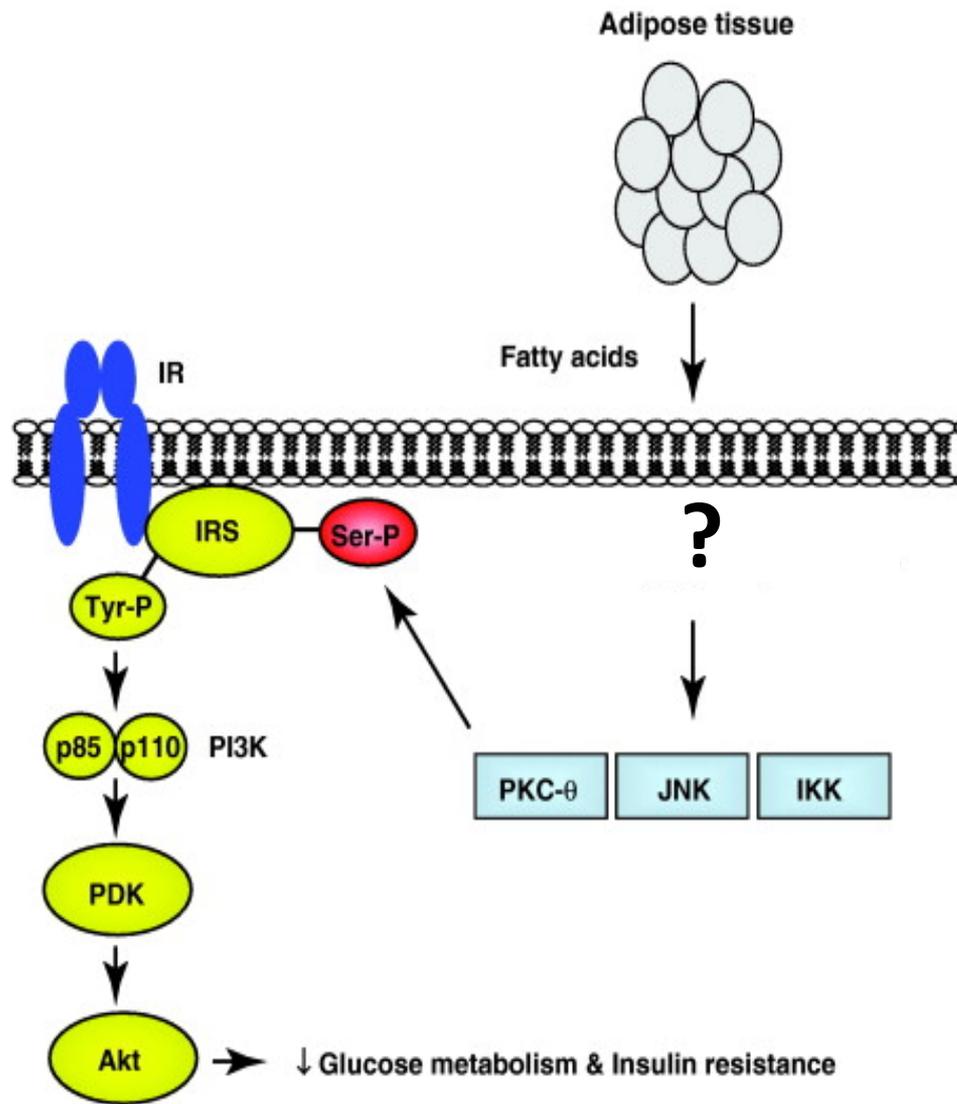


AGL

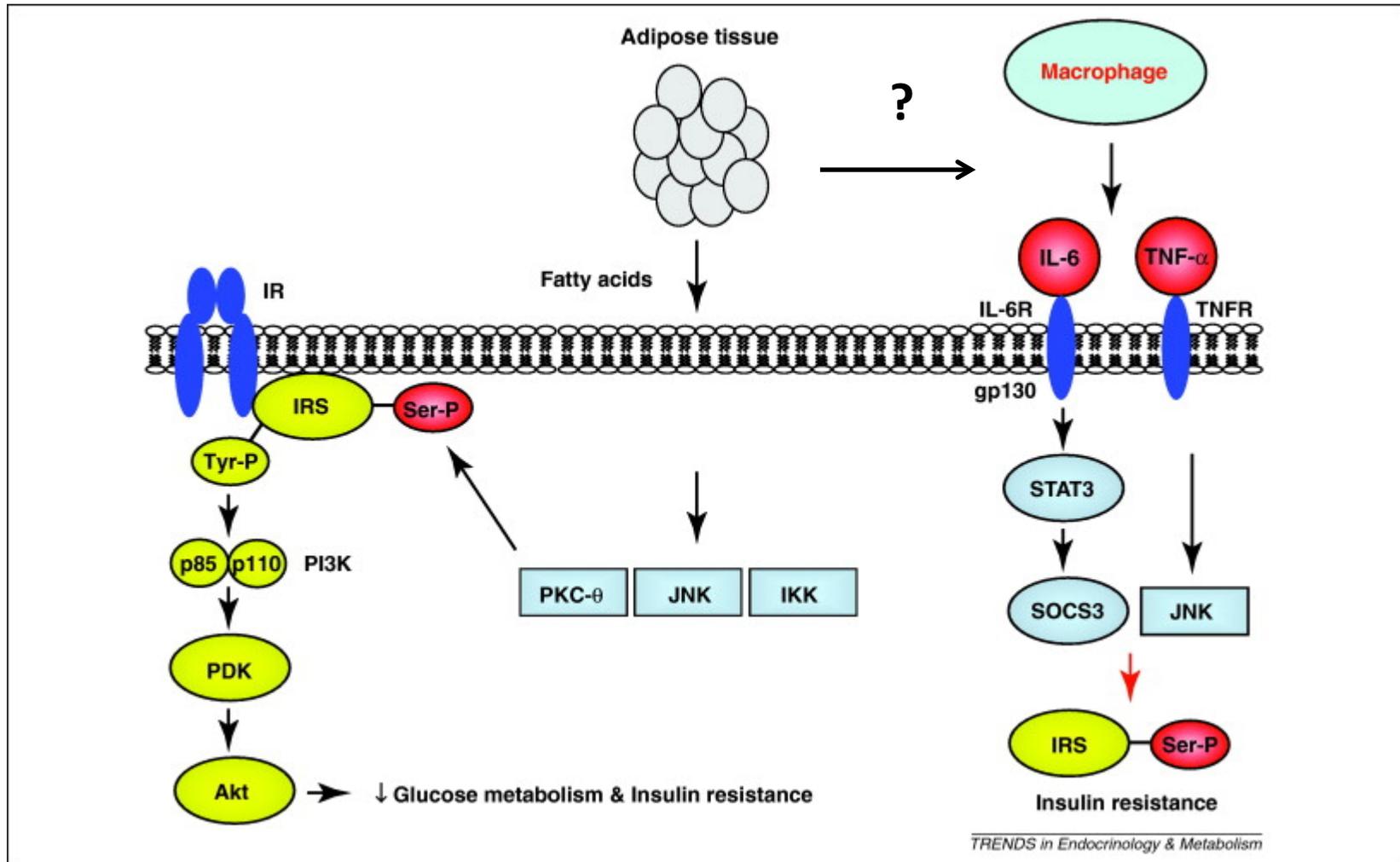


Teoria Portal

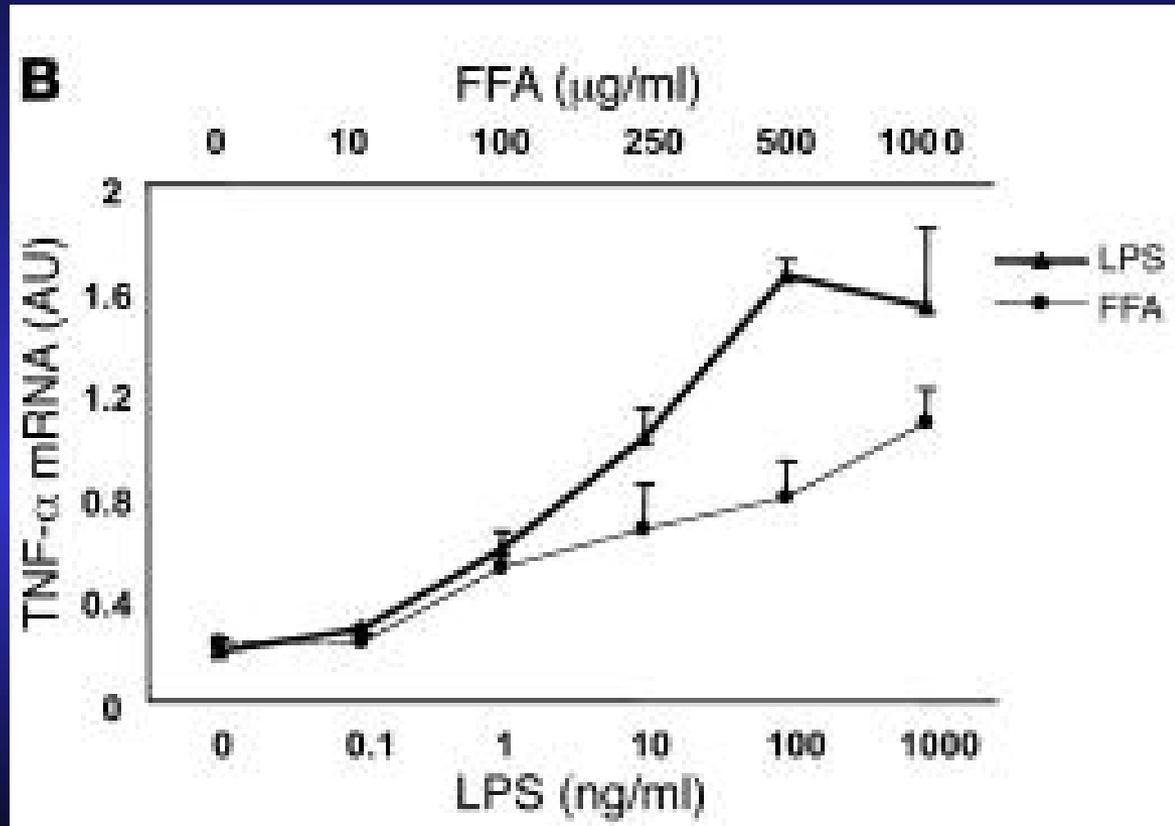
**Teoria do
Vazamento**



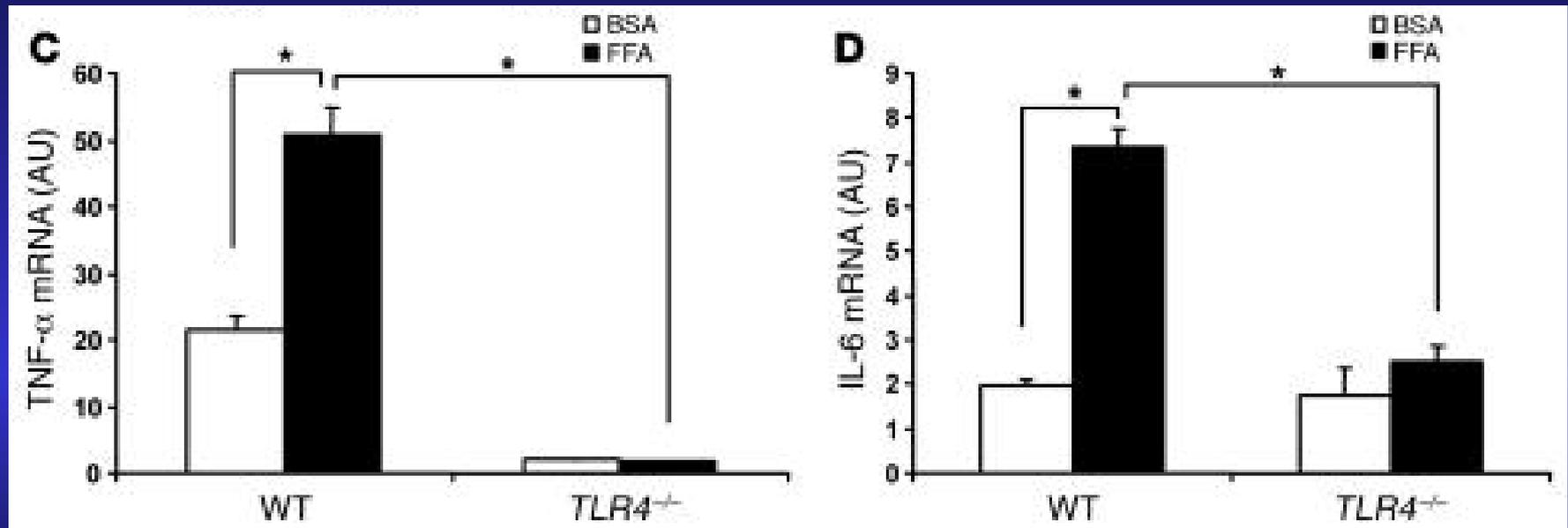
A obesidade é caracterizada por um estado de inflamação crônica



Os AGLs ativam vias inflamatórias em macrófagos



O TLR-4 é o elo de ligação entre os AGLs e a inflamação em adipócitos



Adipocinas

(proteínas secretadas pelos adipócitos)

Leptina ↑

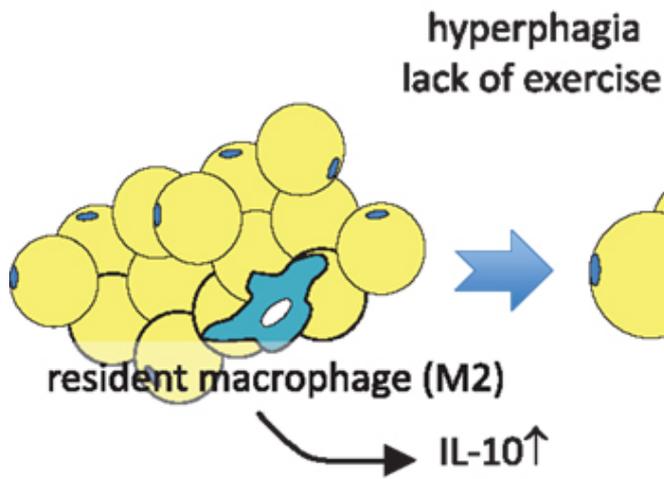
Resistina ↑

Adiponectina ↓

IL-6 ↑

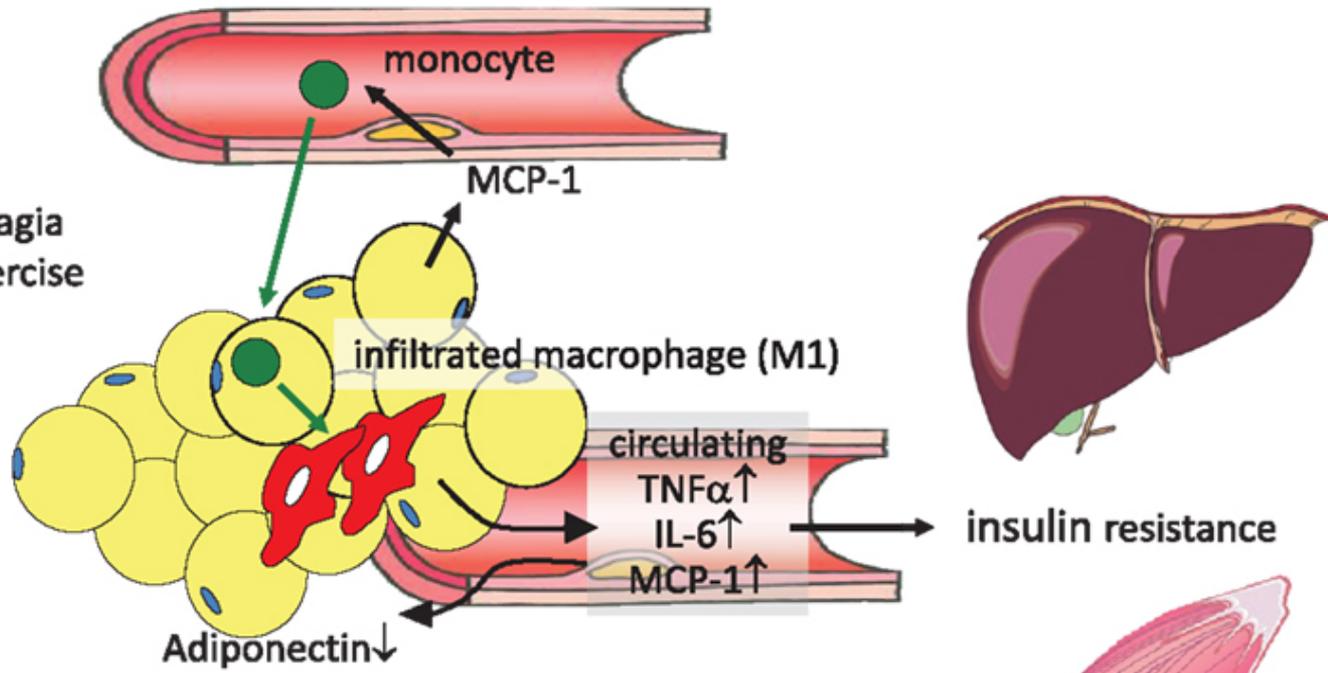
TNF-alfa ↑

A Lean state



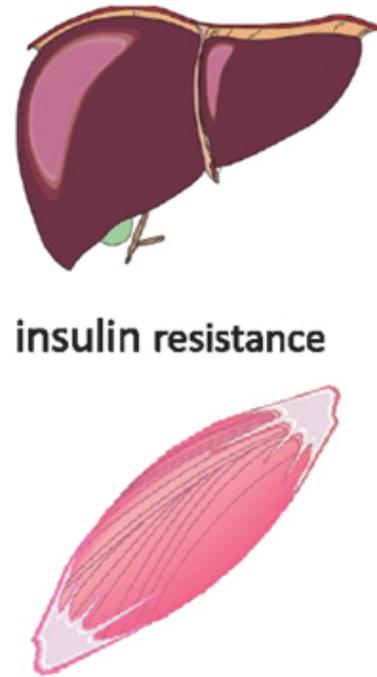
normal adipocytes

B Obese state



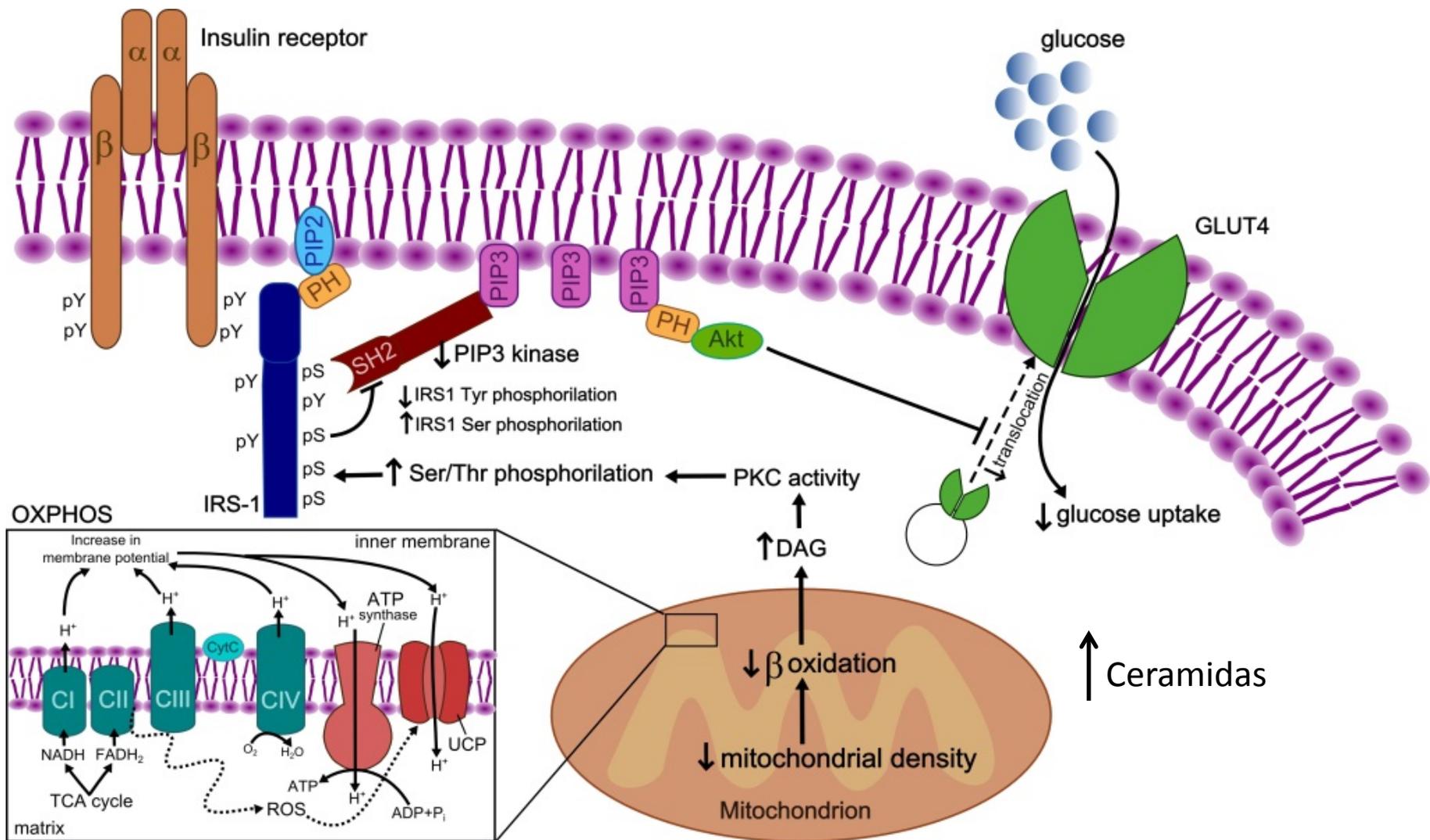
hypertrophied adipocytes

insulin-sensitive tissues

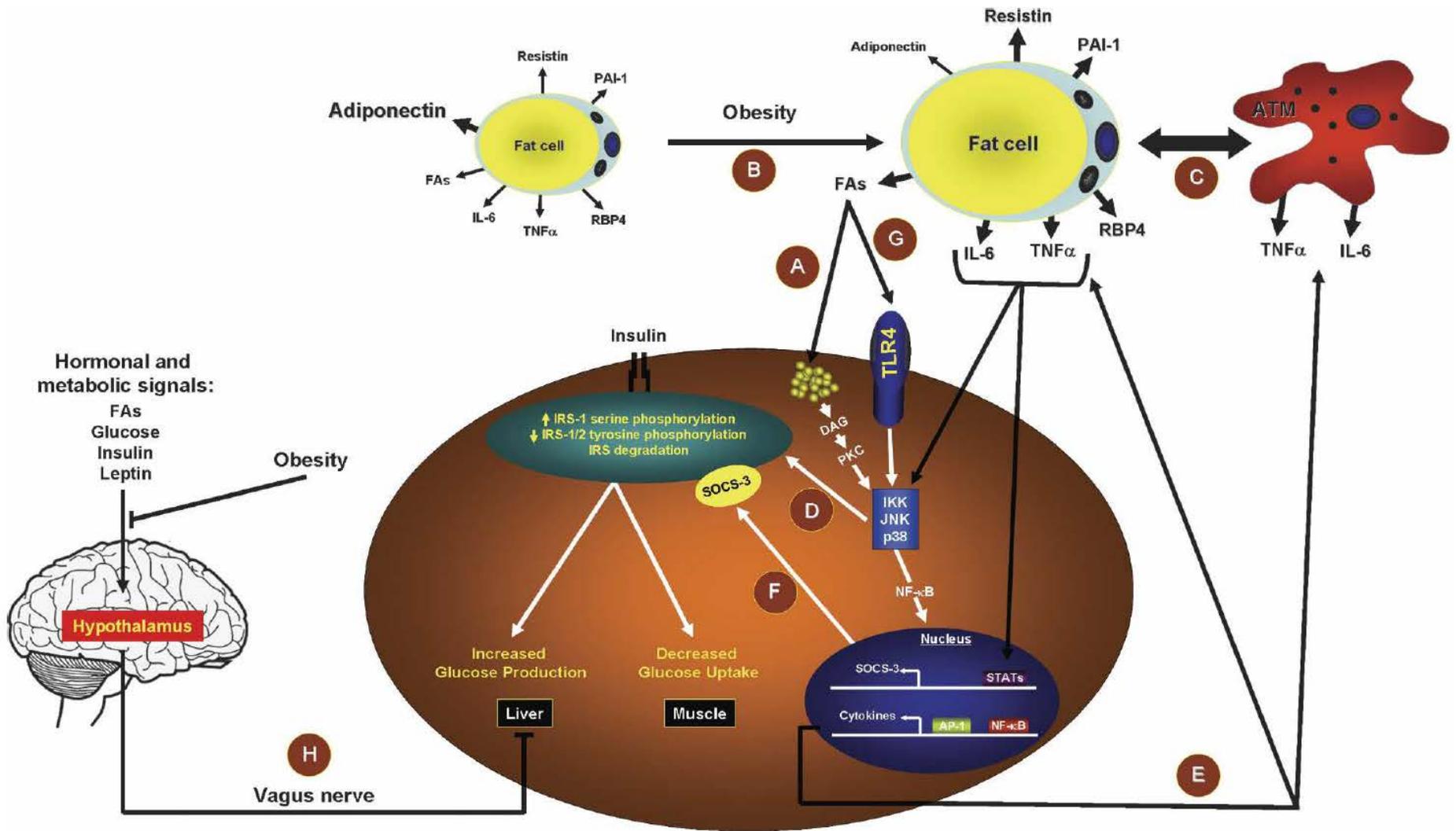


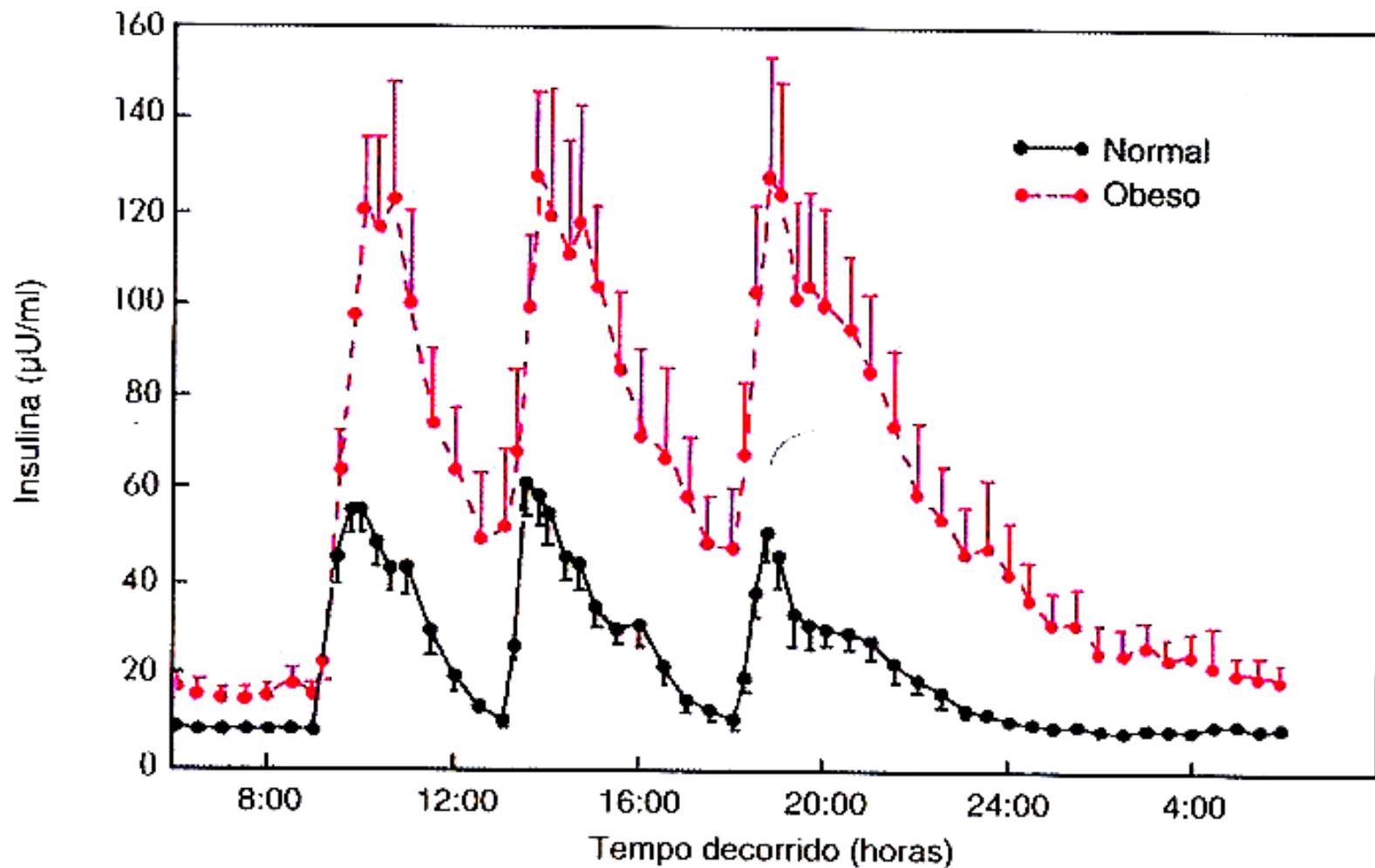
LIPOTOXICIDADE

É uma alteração funcional de tecidos não adiposos causada por reações tóxicas secundárias ao acúmulo de lipídios e seus metabólitos que podem levar à disfunção mitocondrial e à morte celular.



Patogênese da RI em obesos: Sinais hormonais, neurais e inflamatórios



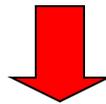


OBESIDADE



RESISTÊNCIA PERIFÉRICA

HIPERINSULINISMO



IDADE



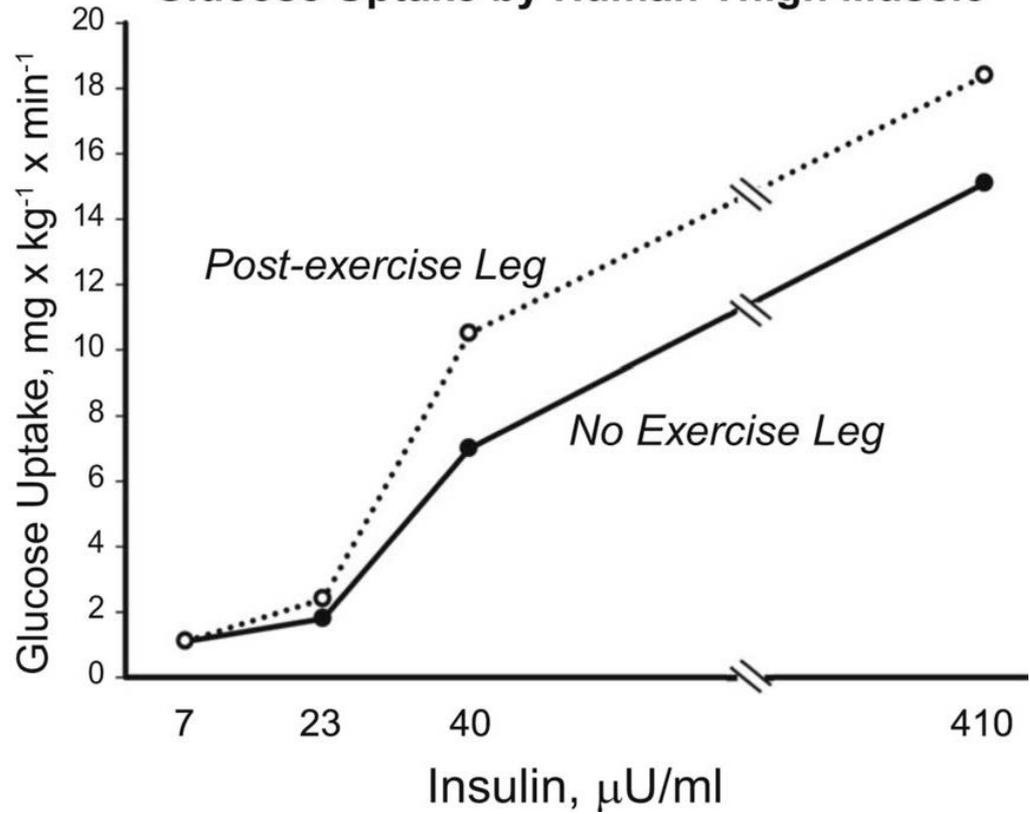
FALÊNCIA CÉLULA β

GENÉTICA

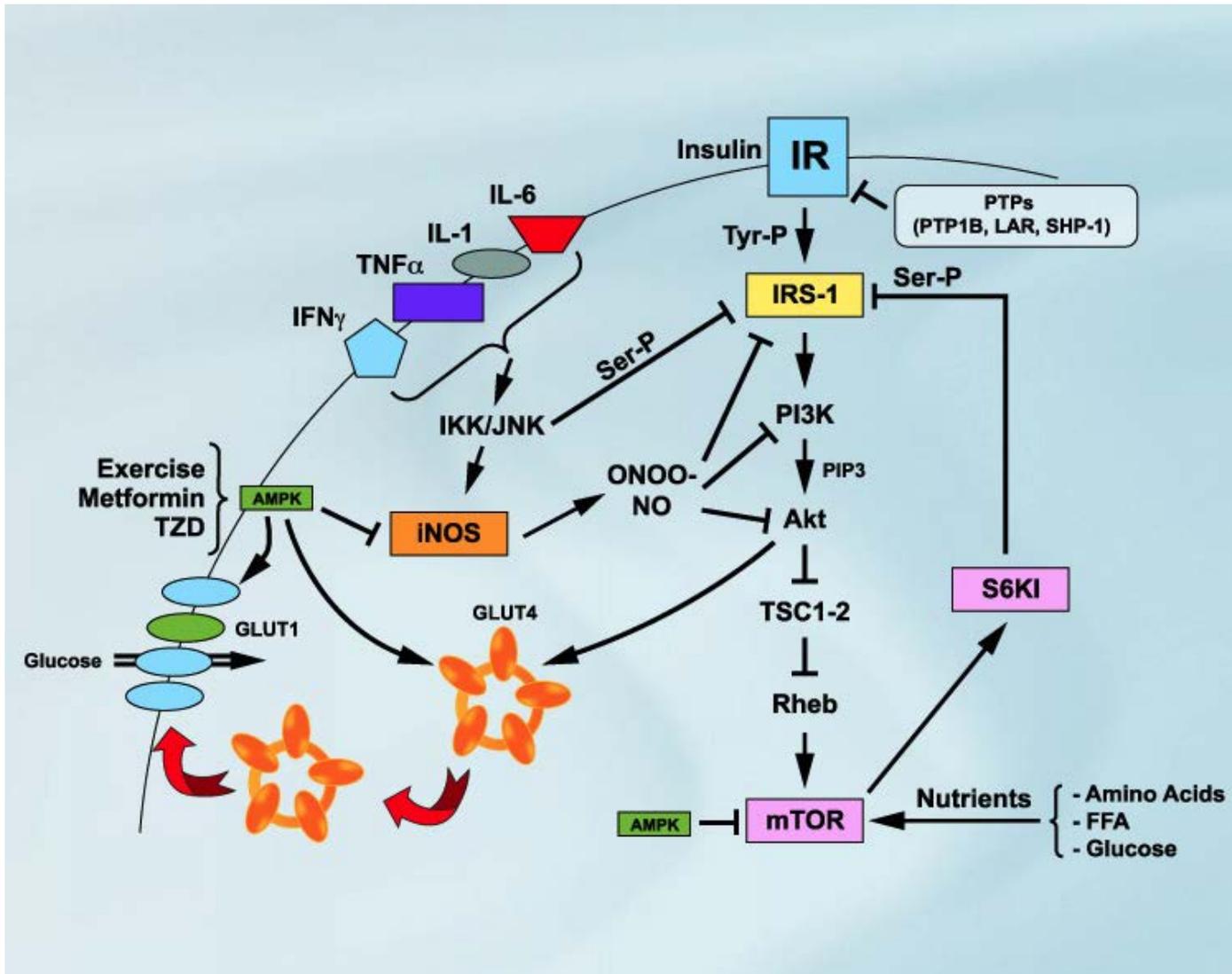


**Como combater o
problema ?**

Glucose Uptake by Human Thigh Muscle



Papel da AMPK na RI



O Exercício reduz a gordura ectópica e tem efeito antiinflamatório

